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BLOOD-CULTURES DURING LIFE IN INFANTS AND YOUNG CHILDREN, WITH DESCRIPTION OF A NEW TECHNIC *

MARTHA WOLLSTEIN, M.D., AND EDWARD MORGAN, M.B.
NEW YORK

Blood cultures made during life in young infants may be an aid to diagnosis or to prognosis, or they may be useful in the study of a given disease from the purely scientific standpoint, with a view to an ultimate practical or therapeutic application. In either case a safe and simple technic is a matter of necessity. It is probably true that the difficulties hitherto encountered in obtaining blood from young infants in quantities sufficient to make the cultural results of value are responsible for the lack of application of the measure in routine practice. The literature on the subject is very meager and is confined almost entirely to cultures taken from older children. In Churchill and Clark's[1] series of sixty-three blood cultures taken from children during life, only nine were under 2 years of age and none was under 12 months. They obtained the blood from a vein in the arm, as did Rotch and Low,[2] whose series does not include any infant less than 2 years old. Delestre[3] obtained 1 to 2 c.c. of blood from the great toe after disinfecting and incising the skin. His studies were made on forty infants ranging from a few days to 4 years of age. Slavyk[4] took the blood from the lobe of the ear, using only a few drops to make the cultures. Neither one of these methods is above criticism, and to enter a vein at the elbow without exposing the vessel by incision is a matter of impossibility in all but a very small number of young infants, whether they are well or poorly nourished. We believe that the method followed by us is an improvement on any which has been previously reported, and therefore the details of the procedure are given.

*From the Pathological Laboratory of the Babies' Hospital.

1. Churchill and Clark: Am. Jour. Dis. Child., 1911, i, 193
2. Rotch and Low: Jour. Am. Med. Assn., 1907, xlviii, 185
3. Delestre: Ann. de gyn. et obst., 1901, lv, 51.
4. Slavyk: Jahrb. f. Kinderh., 1901, liii, 505.

TECHNIC

The blood was taken from the external jugular vein in all the cases in the series except three. In the three exceptions the vein chosen was the superficial temporal in two cases and the median basilic in one.

The patient having been tightly wrapped in a sheet to secure the arms at the sides and prevent struggling, was placed on a table. The head was turned to one side, hyperextended over the end of the table and supported in that position by an assistant. This served the double purpose of making the site of operation more accessible and of facilitating the direct introduction of the needle by tightening the skin over the vein.

The operator's hands were sterilized in the usual manner. The site of aspiration was washed with alcohol and dried, after which tincture of iodin was applied and allowed to remain for three minutes. In few cases was the vein so obscured as to necessitate the removal of the iodin before puncture. The entrance into the vein was most readily effected during a paroxysm of crying when the vessel was distended. Digital pressure above the clavicle we have found to be practically valueless in increasing the prominence of the vein.

A 2-c.c. Luer syringe was used with a 22-gauge needle 1.5 cm. in length. The needle was inserted into the vein in the direction of the blood current and 1 c.c. of blood was drawn off and transferred directly to 30 c.c. of bouillon. It is important that the concentration should not be greater than one in twenty or thirty in order to avoid bactericidal action of the blood. Broth of a reaction of + 0.5 per cent. of phenolphthalein was used in making these cultures and we believe that fluid media give better results than do solid ones.

Three points in the technic are worth emphasizing: the iodin should remain on for at least three minutes before puncture; the puncture should be performed through the iodin whenever possible; it is essential that the vessel be entered with the least possible manipulation in order to avoid contamination from the deeper layers of the skin.

Failures are encountered rarely. With a little practice it is surprising how few attempts end unsuccessfully provided a vein is distinctly visible. There are, however, exceptional cases, usually fat, well-nourished babies, in which the vein is completely obscured by the subcutaneous fatty tissue. None of the children showed any ill effects attributable to the operation, and hemorrhage in the form of a hematoma was not encountered unless the needle transfixed the vessels. The size or prominence of the vein is seemingly not dependent on the age of the child. The small marasmus babies as a rule had prominent veins, whereas difficulties were sometimes encountered in the older, well-nourished children.

The ages of the children in the series varied from 10 days up to 4 years; sixteen children, or 20 per cent., were under 6 months old; twenty-three, or 28.7 per cent., were between 6 months and 1 year; twenty-one, or 26.3 per cent., between 1 and 2 years; four children, or 5 per cent., were between 2 and 3 years old; and sixteen, or 20 per cent., were over 3 years of age. Two babies were only 10 days old, and nearly half the children studied were under 1 year of age, while 75 per cent. were under 2 years. One hundred cultures were made on eighty children. Twenty-six cases, or 32.5 per cent., gave positive results, while fifty-four cases, or 67.5 per cent., gave negative cultures.

The clinical diagnosis varied as Table 1 shows.

LOBAR PNEUMONIA

There are thirteen cases of lobar pneumonia in our series, in four of which the pneumococcus was found in the blood, accompanied in one instance by *Bacillus influenzæ*. All of the thirteen children recovered, so that the blood-cultures were of no prognostic value in this series. All four positive cultures were obtained before the crisis, though in six of the negative cases the blood was also taken while the temperature was still high. None of these patients developed empyema or any other complication. Otten[5] found the pneumococcus in the blood in nine of the seventy cases of lobar pneumonia studied in older children. Of the nine positive cases five children died and four recovered. Churchill and Clark found four positive cases among fifteen lobar pneumonias examined. In two of our positive cases the patients were 9 months old, one was 17 months and one was 3 years of age.

The case of the child whose blood contained both pneumococci and influenza bacilli is of interest. He was 9 months old. On the fourth day of the disease his blood gave a negative culture; on the ninth day it was found to contain both organisms, and on the twelfth day it was negative again. His crisis came on the fourteenth day and the child recovered without complications. This fact is especially interesting because the influenza bacillus isolated from his blood was virulent for rabbits, proving that influenzal bacteriemia of pulmonary origin may be due to a virulent strain of *B. influenzæ* and may run its course without the occurrence of meningitis. Thus Cohen's[6] separation of the influenza bacillus from the *Bacillus meningite cérébrospinale septicémique* would seem to be unnecessary. Influenza bacilli were also isolated from the bronchial secretion of this infant.

5. Otten: Jahrb. f. Kinderh., 1909, lxix, 568.
6. Cohen: Ann. de l'Inst. Pasteur, 1909, xxiii, 273.

TABLE 1.—SHOWING BLOOD CULTURES IN A VARIETY OF DISEASES

Case No.	Age, Months	Sex	Diagnosis	Organism Found	Results
1	30	F	Malignant endocarditis	Streptococcus	Died
2	7	M	Broncho-pneum. and meningit.	Streptococcus	Died
3	9	M	Broncho-pneum. and empyema	0	Died
4	1/3	M	Meningeal hemorrhage	0	Died
5	9	M	Lobar pneum. and septic arthr.	Pneumococcus	Cured
6	19	F	Septic arthritis and meningitis	Streptococcus	Died
7	48	M	Lobar pneum. and empyema	Pneumococcus	Cured
8	7	M	Broncho-pneumonia	0	Died
9	11½	F	Epidemic meningitis	0	Cured
10	42	M	Lobar pneumonia and empyema	0	Cured
11	18	F	Broncho-pneumonia	0	Died
12	2	F	Broncho-pneum. and empyema	Streptococcus	Cured
13	36	F	Lobar pneumonia	0	Cured
14	5	F	Retropharyngeal abscess	0	Died
15	18	M	Double empyema	Pneumococcus	Died
16	15	M	Broncho-pneumonia	Pneumococcus	Cured
17	4½	M	Broncho-pneumonia	0	Died
18	36	F	Lobar pneumonia	Pneumococcus	Cured
19	24	M	Lobar pneumonia	0	Cured
20	22	M	Lobar pneum. and empyema	Pneumococcus	Died
21	6	F	Erysipelas	Streptococcus	Died
22	18	F	Broncho-pneumonia	0	Died
23	8	F	Tuberculous meningitis	0	Died
24	54	F	Tuberculous meningitis	0	Died
25	2½	M	Broncho-pneum. and empyema	Pneumococcus	Died
26	36	M	Exacerbation of old endocarditis	0	Improved
27	5	M	Tuberculous meningitis	0	Died
28	14	F	Lobar pneumonia	0	Cured
29	13	F	Broncho-pneumonia	0	Died
30	42	M	Chorea	0	Cured
31	9	M	Septic arthritis of hip	0	Cured
32	8½	F	Marasmus and nasal diphtheria	Klebs-Loeffler Bac.	Died
33	15	M	Broncho-pneumonia	0	Cured
34	36	M	Congenital heart malformation	0	Unimproved
35	42	F	Rheumatic endocarditis	0	Died
36	36	M	Pulmonary tuberculosis	0	Unimproved
37	48	F	Rheumat. endo- and pericarditis	0	Died
38	13	F	Empyema	Pneumococcus	Cured
39	42	M	Empyema	0	Cured
40	8	F	Acute nephritis	0	Died
41	10	F	Broncho-pneum. and pertussis	0	Unknown
42	14	M	Lobar pneumonia	0	Cured
43	8	M	Pneumococcus meningitis	Pneumococcus	Died
44	11	M	Broncho-pneum. and measles	0	Died
45	17	M	Lobar pneumonia	Pneumococcus	Cured
46	16	M	Lobar pneumonia	0	Cured
47	9	M	Lobar pneumonia	Pneumococcus and *B. influenzæ*	Cured
48	3	F	Pertussis	0	Unknown
49	2½	M	Broncho-pneumonia	0	Cured
50	15	M	Broncho-pneumonia	0	Died

TABLE 1.—*Continued*

51	20	M	Broncho-pneumonia	0	Died
52	17	F	Broncho-pneumonia	0	Cured
53	2½	M	Marasmus and furunculosis	Pneumococcus	Cured
54	6	M	Pleuropneum. and meningitis	Pneumococcus	Died
55	5	F	Empyema and meningitis	Pneumococcus	Died
56	3	F	Marasmus	0	Improved
57	4	F	Acute bronchitis	0	Cured
58	12	F	Broncho-pneumonia	0	Died
59	12	M	Broncho-pneumonia	0	Cured
60	⅓	M	Pyemia and septic arthritis	Aurococcus	Died
61	6	F	Lobar pneumonia	0	Cured
62	10	F	Broncho-pneumonia	Pneumococcus	Cured
63	36	M	Broncho-pneumonia	Pneumococcus	Cured
64	36	M	Lobar pneumonia	0	Cured
65	42	F	Broncho-pneumonia	0	Cured
66	7½	M	Broncho-pneumonia	0	Cured
67	8	M	Gastro-Intes. intox. and broncho-pneumonia	0	Died
68	6	M	Marasmus	0	Died
69	14	F	Broncho-pneumonia	0	Cured
70	7	M	Broncho-pneumonia	0	Cured
71	9	M	Broncho-pneum. and tetany	0	Cured
72	24	M	Broncho-pneum. and empyema	0	Cured
73	5	M	Empyema and meningitis	Pneumococcus	Died
74	24	M	Lobar pneumonia	0	Cured
75	2	M	Broncho-pneumonia	Streptococcus	Died
76	15	F	Lobar pneum. and empyema	Pneumococcus	Died
77	2	F	Marasmus and cellulitis of scalp	0	Unimproved
78	10	F	Broncho-pneum. and von Jaksch Anemia	0	Unimproved
79	60	M	Empyema	0	Cured
80	18	M	Lobar pneumonia	0	Cured

TABLE 2.—RESULTS OF BLOOD-CULTURES IN LOBAR PNEUMONIA

Case No.	Age, Months	Sex	Day of Positive Cult.	Day of Negative Cult.	Day of Crisis	Organism	Result
5	9	M	*	.....	.....	Pneumococcus	Cured
13	36	F	.....	5th	?	0	Cured
18	36	F	6th	17th	11th	Pneumococcus	Cured
19	24	M	.....	5th	5th	0	Cured
28	14	F	.....	8th	11th	0	Cured
42	14	M	.....	7th	9th	0	Cured
45	17	M	21st	23rd	22nd	Pneumococcus	Cured
46	16	M	.....	6th	7th	0	Cured
47	9	M	9th	4th and 12th	14th	Pneumococcus and *B. influ.*	Cured
61	16	F	.....	5th	7th	0	Cured
64	36	M	.....	8th	8th	0	Cured
74	24	M	.....	2d, 4th, 7th	3rd	0	Cured
80	18	M	.....	3d, 4th	4th	0	Cured

*Day of onset unknown.

TABLE 3.—RESULTS OF BLOOD-CULTURES IN BRONCHO-PNEUMONIA

Case No.	Age, Months	Sex	Day of Positive Culture	Day of Negative Culture	Organism	Result
2	7	M	2nd	.....	Streptococcus	Died seventh day.
8	7	M	.....	8th	0	Died tenth day; no autopsy.
11	18	F	.....	2nd	0	Died at home; date not known.
16	15	M	8th	20th	Pneumococcus	Cured.
17	4½	M	.....	9th	0	Died tenth day; heart's blood sterile.
22	18	F	.....	2nd	0	Died second day; no autopsy.
29	13	F	.....	15th	0	Died nineteenth day; heart's blood sterile.
33	15	M	.....	6th	0	Cured.
41	10	F	.....	4th	0	Left hosp. and could not be found.
44	11	M	.....	7th	0	Died, no autopsy.
49	2½	M	.....	8th	0	Cured.
50	15	M	.....	1st	0	Died second day; heart's blood sterile.
51	20	M	.....	9th	0	Died; no autopsy.
52	17	F	.....	5th	0	Cured.
54	6	M	12th	.....	Pneumococcus	Died fourteenth day; no autopsy.
58	12	F	.....	11th	0	Cured.
59	12	M	.....	6th	0	Cured.
62	10	F	7th	17th	Pneumococcus	Cured.
63	36	M	3rd	11th	Pneumococcus	Cured.
65	42	F	.....	15th	0	Cured.
66	7½	M	.....	1 month after onset	0	Cured.
69	14	F	.....	15th	0	Cured.
70	7	M	.....	7th	0	Cured.
71	9	M	.....	21st	0	Cured.
78	10	F	.....	4th	0	Cured.
75	2	M	4th	.....	Streptococcus	Died.

TABLE 4.—RESULTS OF BLOOD-CULTURES IN EMPYEMA

Case No	Age, Months	Sex	Day of Positive Culture after onset of Pneumonia	Day of Negative Culture	Organism	Result
3	9	M	.....	15th	0	Died thirtieth day; blood at autopsy streptococcic.
7	48	M	26th	28th	Pneumococcus	Cured.
10	42	M	.....	28th	0	Cured.
12	2	F	9th	.....	Streptococcus	Cured.
15	18	M	26th and 30th	40th	Pneumococcus	Died eight weeks after onset of pneumonia.
20	22	M	21st	18th	Pneumococcus	Died twenty-seventh day. Heart's blood at autopsy pneumococcic.
25	2½	M	14th*	.....	Pneumococcus	Died five weeks after onset pneum.
38	13	F	8th	11th	Pneumococcus	Cured.
39	42	M	.....	10th	0	Cured.
55	5	F	Over 3 weeks	.....	Pneumococcus	Died same day.
72	24	M	.....	2 months	0	Improving.
73	5	M	16th	.....	Pneumococcus	Died same day.
76	15	F	4th and 6th	.....	Pneumococcus	Died. No autopsy.
79	60	M	.....	21st	0	Improving.

*Nineteen days before empyema was discovered.

BRONCHOPNEUMONIA

Twenty-six cases of bronchopneumonia were studied, with six positive results. The pneumococcus was found four times and the streptococcus twice. Both children with streptococcus and one with pneumococcus infection died, while three pneumococcus patients recovered. The cocci were found in the blood on the second, fourth and twelfth days in the fatal cases and on the third, seventh and eighth days in the patients who recovered. So that no prognostic value could be ascribed to the date of positive blood-cultures in these twenty-six cases. Eight of the children in the negative series died, a slightly lower mortality-rate than obtained in the positive cases. Churchill and Clark found the pneumococcus in one of three lobular pneumonia cases.

EMPYEMA

Fourteen children with empyema gave positive blood-cultures nine times; in all but one the pneumococcus was the bacterium found. Six children among the positive cases died, while only one of the negative cases resulted fatally. Three of the infants with positive cultures had pneumococcus meningitis as well as empyema. It would seem, then, that bacteriemia in this series of empyema patients was a bad prognostic sign in about 55 per cent. of the cases, and that it sometimes meant infection of another serous membrane. The single example of streptococcus empyema in this series of cases recovered. The subject was a baby only 2 months old. It is probable that all these cases of empyema followed pneumonia, but as the majority of them were admitted with pus in the chest it was not always possible to diagnose the type of pneumonia preceding the pleurisy. Bronchopneumonia was present in five children, lobar pneumonia in four and in five cases the type was not diagnosed. Four of the children with bronchopneumonia died, only three having given a positive blood-culture; while of the empyema cases following lobar pneumonia two children died, both having had a pneumococcus bacteriemia.

MENINGITIS

Six cases of meningitis included three of the tuberculous form, one of the meningococcus, one of the pneumococcus, and one of the streptococcus varieties. The last two gave positive blood-cultures; the other four did not. The child with meningococcus meningitis recovered after treatment with antimeningococcus serum. All the rest were fatal, as was to be expected, the meningitis being the terminal lesion in a general infection.

RHEUMATISM

There were four cases of rheumatism in children 3 and 4 years old. None gave a positive blood-culture though two children had acute endocarditis, one had an acute exacerbation of an old endocarditis, and one had chorea. Two patients died, but only one came to autopsy, and her heart's-blood after death gave no growth.

OTHER POSITIVE CASES

In one case of malignant endocarditis the child had a streptococcus bacteriemia and died on the twenty-fifth day of the disease.

A case of erysipelas gave a negative blood-culture on the sixth and seventh days of the disease, but on the eleventh day the streptococcus was found in the blood and the patient died on the seventeenth day.

The only case in which the aurococcus was found in the blood was a child 10 days old, who had been admitted with omphalitis and suppurative arthritis of the wrist from which the same organism was grown. The baby died.

Two marasmic infants are of interest. One had furunculosis. He was 2 months old and pneumococci were found in his blood though his temperature was normal at the time the culture was taken. He recovered. The other child was 8 months old and had nasal diphtheria. *B. diphtheriæ* was found in pure culture in her blood. She died but no autopsy was permitted. The case will be reported in detail later.

SUMMARY

Blood for bacteriologic examination was readily obtained from the external jugular vein in infants as young as 10 days of age.

The pneumococcus was found before the crisis in the blood in four out of thirteen cases of lobar pneumonia (30.8 per cent.), all of which patients recovered.

A bacteriemia was demonstrated in six out of twenty-six cases of bronchopneumonia (23 per cent.), the pneumococcus being recovered in four and the streptococcus in two. Both streptococcus patients died and one pneumococcus case also proved fatal. In eight bronchopneumonia cases without bacteriemia the patients also died.

The highest percentage of positive blood-cultures was found in cases of empyema: nine of fourteen, or 64.3 per cent. But even in empyema bacteriemia does not necessarily mean a fatal prognosis, as in 33.3 per cent. of the positive cases the children recovered.

THE PANCREATIC FERMENTS IN INFANTS*

ALFRED F. HESS, M.D.
NEW YORK

For many years our lack of knowledge of the processes of intestinal digestion, and of the action of the glands which line the wall of the intestine, as well as those which pour their secretions into it, has hindered the study of the metabolic processes during infancy. It has frequently been regretted that we have to content ourselves with a direct study of the activities of the stomach, and cannot gain similar direct access for an investigation of the intestine, of the pancreas and of the liver. From time to time ingenious methods have been devised to overcome the inaccessibility of this region, and although most of these have proved of doubtful value, and hardly any have been satisfactorily applied to infants, it may be well to review them briefly.

The first methods were based on the principle of giving a food by mouth in such a form that it could not be digested by the stomach, and of subsequently examining the stool to judge of the efficiency of the intestinal digestion. Sahli's glutoid capsule and Schmidt's nuclear tests based on this principle were devised to test the tryptic activity of the pancreas. However, as it has been shown that the capsules are dissolved when given to dogs deprived of the pancreas,[1] and as Schmidt's test is also not reliable, the advisability of adapting these tests to our purposes may be dismissed.

A second method of investigation consists in examining the stool for the ferments themselves, especially for trypsin, but also for amylase, and for lipase or for the products of fat splitting. Many investigations have been carried out in this way to ascertain the secretion of trypsin. For this purpose the Müller-Schlecht[2] method, which depends on the digestion of serum, or the Volhard[3] and Gross[4] method, in which casein is substituted for serum, has been employed. A method of estimating the activity of intestinal diastase is also based on the above principles, and consists of a test introduced by Wohlgemuth[5] to judge of the starch-converting power of the stool. Similarly, but with less success, the stools have been examined for lipase, but more frequently for their content of free fat, fatty

*From the Research Laboratory, Department of Health, New York City.

1. Frank, F.: Arch. f. Verdauungskr., 1912, xviii.
2. Schlecht, H.: München. med. Wchnschr., 1908, xiv, 725.
3. Volhard, F.: München. med. Wchnschr., 1907, 403.
4. Gross, O.: Arch. f. exper. Path. u. Pharmakol., 1908, lviii, 157.
5. Wohlgemuth, J.: Berl. klin. Wchnschr., 1910, p. 92.

acids and soaps. The Cammidge reaction of the urine, said to be a test for glycerin, a product of fat-splitting, may be passed over with mere mention.

Still another principle is involved in the test of Boldyreff.[6] This consists in giving the patient oil by mouth, an oil-breakfast, which excites a regurgitation of pancreatic fluid into the stomach. The stomach contents are evacuated and tested for the pancreatic ferments. We have seen but one report of a test by this method on an infant, and in that case it was not successful.[7] One of the difficulties is that the regurgitation from the duodenum does not always follow. Moreover, in infants it would seem to be of doubtful value, on account of the necessity of putting a large amount of oil into the stomach.

One valuable source of information which has been grasped by those interested in this phase of physiology or pathology, is the occasional fistulæ of the pancreas or of the small intestine, which allow of the collection of their secretions. However, this exceptional opportunity, which has been taken advantage of from time to time since the famous observations of Beaumont in 1833, has never been accessible to those desirous of making a similar study on an infant.

The greatest advance in method has been made recently by the use of duodenal tubes. Almost simultaneously Gross[8] and Einhorn[9] published an account of a tube which when introduced into the stomach was carried by peristalsis into the upper intestine. Hemmeter[10] had attempted to use this direct method some years before. By means of this direct method, Einhorn and Rosenbloom[11] made a study of pancreatic ferments in the adult, which will be referred to below.

About two years ago a duodenal tube modelled after the Gross tube was devised for use on infants, and the early part of this study was carried out with its aid. It was found, however, that the method could be modified and greatly simplified for infants; that a simple catheter could be employed for these examinations. This duodenal catheter has been described in the pages of this journal in connection with the diagnosis and treatment of pylorospasm,[12] and in a study of icterus neonatorum.[13] It has also been briefly described in a paper on the bacteriology of the duodenum in infants,[14] and elsewhere,[15] so that it is unnecessary

6. Boldyreff, W.: Zentralbl. f. d. ges. Physiol. u. Path. d. Stoffwechs., 1908, p. 209.
7. Ibrahim, J.: Verhandl. d. Deutsch. Naturf. u. Aertzte, 1908, p. 316.
8. Gross, M.: New York Med. Jour., 1910, No. 2.
9. Einhorn, M.: Med. Rec., New York, 1910, No. 3.
10. Hemmeter: Complete reference not supplied.
11. Einhorn, M., and Rosenbloom, J.: Arch. Int. Med., 1910, p. 667.
12. Hess, A. F.: Amer. Jour. Dis. Child., 1912, p. 133.
13. Hess, A. F.: Amer. Jour. Dis. Child., 1912, p. 304.
14. Hess, A. F.: Jour. Infect. Dis., July, 1912, p. 71.
15. Hess, A. F.: Arch. Int. Med., 1912, p. 37.

here to enter into the technic of its use. The catheter was used in this study of the pancreatic ferments because it seemed certain that an advance in our knowledge could be made by means of this method, which must be of greater value than the indirect methods which have preceded it. Just as it is preferable to test for rennet and for pepsin the stomach contents rather than in the stool, so in the case of the pancreatic ferments it is preferable to examine the duodenal contents rather than the stool. In the stool we have leukocytic ferments, bacterial ferments and other cellular ferments which possess proteolytic activity and are readily confused with trypsin. Schlecht's[2] report of the digestion of serum by means of a solution of old, thoroughly dried stool would even suggest activity other than ferment action, as a cause of proteolysis. In addition to the fact that the pancreatic ferments are mingled with non-pancreatic ferments in the feces — for besides these cellular enzymes, many others, for example, intestinal lipase, erepsin and probably intestinal amylase appear in the stool — the material for examination must naturally be contaminated with unutilized food products. But of more weight is the fact that we have no means whatsoever of even estimating how much ferment has been absorbed or utilized in the small intestine. That this factor is large we can infer from our knowledge that this part of the intestine is the seat of the physiologic activity of these ferments, and that they must be largely used up in this process. Experiment confirms us in this opinion, for it has been demonstrated that the ferments of the pancreas are hardly present in chyme obtained from a fistula in the cecal end of the ileum.[2] Realizing this defect in method, and in order to allow as little time as possible for absorption, a cathartic is given before obtaining stools for the ferment tests.

Such are the criticisms which justly can be levelled at any tests of stool for pancreatic ferments, but which a direct duodenal test is not exposed to. However, the direct method which we have used in this study, like most methods, is likewise not perfect. It may truly be argued that the duodenal fluid may suffer an admixture of gastric juice. At present this cannot be obviated; however, if all duodenal fluid which is acid is discarded, and only alkaline or neutral juice examined, this objection loses much of its force. We should realize also that the pancreatic juice obtained in this way cannot be considered pure, as it contains bile as well as some succus entericus. These criticisms would apply forcibly were we pursuing a purely chemical study of pancreatic enzymes. However, we have not undertaken a study of this nature, but rather an investigation of the activity of duodenal digestion, in which the pancreatic ferments take a pre-eminent part, and the bile and other juices play a minor but by no means negligible rôle. Moreover, there is no other way in which a pancreatic juice even comparatively pure can be obtained.

When we inquire into the present status of our knowledge in regard to the activity of the secretions of these glands in infancy, we find that one of the most modern and exhaustive books on the physiology of the digestion of the infant, that of Czerny and Keller,[16] confines itself largely to a discussion of the results of post-mortem investigations, "in view of the fact that the secretions of the intestinal glands and the functions of these secretions are not accessible to direct examination *intra vitam*." Tests of this nature, made with the watery extract of a gland, have a very limited application to the physiologic activity of an organ, and can be considered of only temporary value in lieu of something better. This becomes all the more evident when we reflect that merely the proferment may exist in the gland parenchyma, and that an activating substance, such as enterokinase in the case of trypsinogen, may be necessary to render the ferment potent. We shall have occasion to refer to these investigations based on post-mortem material, and also to those undertaken by means of the examination of the stool. There has been no direct test of the pancreatic ferments of infants.

TECHNIC OF CHEMICAL TESTS

The fluid was brought to the laboratory as soon as possible, generally within an hour or two and subjected to the following tests:

Amylase Test: One c.c. of duodenal fluid was added to a tube containing 10 c.c. of freshly prepared 1 per cent. starch solution, and 1 c.c. of toluol. A control tube contained only starch solution and toluol. Both were placed in the thermostat at 37 C. for forty-eight hours. The mixtures were then made up to 50 c.c. by the addition of water, and run from a burette into 10 c.c. of Fehling's solution (Fehling's solution equals 5 c.c. of the alkaline solution, plus 5 c.c. of the copper solution, plus 30 c.c. water). Ten c.c. of this solution represents 0.002 gm. of glucose. As an indicator of the complete reduction of the Fehling's solution concentrated potassium ferrocyanid (2 to 3 c.c.) and glacial acetic acid (a few drops) were used.

Lipase Test: One c.c. of the duodenal fluid was added to 1 c.c. neutral ethyl butyrate, 1 c.c. toluol, 10 c.c. water. As controls a test of the duodenal fluid and one of the ethyl butyrate were made. The three tubes were incubated for twenty-four hours, and titrated against N/20 NaOH, using phenolphthalein as an indicator. The acidity of the duodenal fluid, and of the butyrate solution, was then deducted to obtain the net amount of acid due to lipolytic action.

Trypsin Test: In the early tests made over a year ago Mett's tubes were used. As is well known, these consist of tubes of small caliber containing coagulated egg-white. These were found serviceable for qualitative tests, but unreliable for quantitative estimations. It was found that tubes of 5 per cent. gelatin were fully as reliable and much more practicable, so that this method was followed in most of the tests. To a tube of gelatin 0.5 c.c. of duodenal fluid, 0.5 c.c. of toluol, as well as 0.25 c.c. of N/1 NaOH were added. The control consisted of a tube containing gelatin, sodium hydrate, and toluol. Tubes prepared in this way were incubated generally for twenty-four and for forty-eight hours, and then placed in the refrigerator. The time necessary for liquefaction was noted, and

16. Czerny, A., and Keller, A.: Des Kindes Ernährung, etc., 1906, i, 66.

also whether this change was complete or incomplete. Casein was not used in these tests as it is well known that it is reacted on by erepsin as well as by trypsin.

In addition to these chemical tests the amount, the color, the consistency and the reaction of the fluid to litmus and to phenolphthalein were noted. At the time of the passing of the catheter, the amount of the stomach content, its reaction to litmus and to Congo paper, were recorded, as well as various secretory and motor phenomena.

SCOPE OF ORIGINAL INVESTIGATION

The following direct study of pancreatic ferments by means of the duodenal fluid may be grouped thus:

1. Normal cases:
    a. Tests before the infant had nursed (during first half day of life).
    b. Tests during first week of life.
    c. Test on older infants (one week to one year).
2. Pathological cases:
    a. Tests in cases of marasmus (atrophy, decomposition).
    b. Tests in cases of pylorospasm associated with gastric hypersecretion.
3. Chemical and physiologic observations on the duodenal secretion.

1. Normal Cases.—a. Tests of Unfed New-born Infants.—The first tests were carried out on infants varying in age from a few weeks to a few months, but it soon became evident that in order to get a comprehensive view of the subject, the ferments ought to be sought from the day of birth, even before they had been put to the breast. Accordingly, a large number of infants were examined by means of the catheter during the first few hours of life, to ascertain whether the pancreatic ferments are present in the duodenum at this period and whether they are secreted independently of the stimulus of colostrum. The passage of the catheter in the new-born is very easily accomplished, as has been recently pointed out in an article on icterus neonatorum. The two investigations were pursued simultaneously; that is to say, the fluid which was aspirated was considered both in regard to the presence of bile and the pancreatic ferments. The examination was by no means always successful, for although access to the duodenum was almost always possible, frequently the upper intestine was empty and no fluid could be aspirated. In a few instances, in these very young infants, a slight admixture of blood rendered the fluid valueless for our purposes; and in some other cases the scanty duodenal contents were rendered acid by an admixture of gastric juice. For these various reasons, although fifty-five tests of the "unfed new-born" were attempted, duodenal juice was obtained in only eleven, and in no instance

in sufficient quantity to make tests for all three ferments, for trypsin, lipase and amylase. However, a test for one ferment was made in one case, and for another in the next, using all the ferment that was secured, with the object of ascertaining whether these pancreatic ferments are present in the intestine before the ingestion of any food.

Before proceeding to detail the results, it will be of advantage to review the previous work in this field; and as the investigations on this group of infants, those who had not nursed, are so few in number, it would seem advisable at the same time to include reports of infants who were somewhat older. The greatest divergence of opinion has always existed as to the time of appearance of amylase. Zweifel,[17] who made use of extracts of the pancreas, failed to demonstrate the ferment in infants under two months of age, and Korowin[18] confirmed these results. Moro,[19] however, repeating this investigation, but making use of an improved technic, more especially by extracting the pancreas for a longer period and at a higher temperature, demonstrated the presence of diastase in the pancreas of an infant which died at birth, and of some others which had lived for a few days. Ibrahim[7] found amylase in the pancreas of the new-born and of the premature infant, and numerous ferments in the meconium.

As is well known, trypsin is not present in the pancreas, but exists in the form of its proferment, trypsinogen, which is activated by the enterokinase of the intestine. Both trypsinogen and enterokinase have been found in the fetus, and trypsin in the stools during the first day of life.[20] Another proteolytic ferment, erepsin, which we shall have occasion to refer to later, has likewise been found in the fetus.[21]

Lipase has been demonstrated in the meconium in small amounts during the first day of life,[20] and, according to Sedgwick,[22] a gastric lipase of considerable lipolytic power may be obtained from the stomach by the second week.

It will be noted that most of these examinations have been made either on post-mortem material, or on infants somewhat older than those comprising our first group. In our experience trypsin and lipase were found most constantly. The former in nine out of eleven tests, and by no means as a mere trace, but sufficient frequently to digest the gelatin in twenty-four to thirty-six hours. Lipase was demonstrated in four of the five tests, also in considerable quantity—from 0.5 c.c. to 2.9 c.c.—as measured by titration with 1/20 N. NaOH solution. Lipase of uncertain origin

17. Zweifel: Untersuch. u. d. Verdauungsapparat d. Neugeb., 1874, p. 35.
18. Korowin, J.: Jahrb. f. Kinderh., 1875, viii.
19. Moro, E.: Jahrb. f. Kinderh., 1898, iii, 342.
20. Hecht, A.: Die Faeces d. Säuglings, 1910, p. 153.
21. Langstein, M. and Soldin, M.: Jahrb. f. Kinderh., 1908, p. 9.
22. Sedgwick, J.: Jahrb. f. Kinderh., 1906, p. 194.

was found in small amount in the stomach contents. Amylase was present twice and absent six times. This positive reaction was not due to an admixture of saliva, for no saliva was present in the material examined; the one case belonged to a series of four, in which a dilute solution of alum was swabbed on the papillæ of the salivary ducts, resulting in complete inhibition of salivary excretion. From these tests we conclude that the three pancreatic ferments are frequently present in the duodenum at or soon after birth. The youngest infant in which amylase was demonstrated was one and a half hours old.

The results of these tests, comprising a narrow field, are of physiologic rather than of clinical interest, and need no clinical commentary. The accepted mechanism of pancreatic secretion is that secretin is elaborated by the mucosa of the small intestine, enters the portal circulation and acts as a hormone to stimulate the pancreas. There is no way of judging whether secretin, in our cases, acted as the messenger to stimulate the pancreatic activity; it has been found in infants which died at birth, but it is not at all times present in the intestine of the new-born. Whatever the mechanism, it is clear that food is not needed to stimulate the activity of the pancreas. The hydrochloric acid which is regularly present in the stomach at birth, as we shall show at another time, would seem to be sufficient to initiate the excretion of pancreatic juice into the duodenum.

b. Tests During the First Week of Life.—Fifty tests were made on thirty-three infants varying in age from one-half to seven days, the same method of examination being employed as in the cases of the former group. Some of these tests did not include an analysis of the duodenal contents, but were made for the purpose of obtaining gastric juice or bile, of determining the state of the pyloric sphincter, or to obtain material for bacteriologic investigation. However, in forty-one instances one or more of the three pancreatic ferments were investigated. As was to be presupposed from our experience with the younger infants, the presence of all three ferments was demonstrated. Trypsin was regularly found in quantity sufficient to digest 5 per cent. gelatin within twenty-four hours; in only two of nineteen tests was it absent. Through an error, 10 per cent. gelatin was used for several of these tests, and as gelatin in this concentration is not applicable as a test for trypsin, these examinations were necessarily discarded.

Lipase was found in all of the ten fluids in which it was tested. In infants one week of age the duodenal juice obtained within an hour is insufficient in amount to carry out the tests with each fluid, for 2 c.c. are necessary for the lipase test, one for the amylase test, and 1.0 c.c. for trypsin. If only a small amount of fluid was obtained, trypsin was tested for, but unless the fluid was neutral or alkaline to litmus, it was not examined for ferments. The lipase varied in quantity from 0.25 c.c. to

2.4 c.c., almost all being under 2.0, as judged by titration with 1/20 N. NaOH.[23] It is not possible to ascribe this variation solely to a difference in the quantity of lipase secreted, as the fluids examined were not sufficiently pure to allow of this deduction. In addition to a difference in the amount of lipase, there are numerous factors which may well have contributed to these varying results. For instance, the dilution of the pancreatic lipase with succus entericus or with gastric juice; the presence of more or less bile, which would tend to dilute the pancreatic secretion, although at the same time augmenting its lipolytic action; the variation in the reaction of the juices. Experiments undertaken at the outset of this work clearly demonstrated that a slight addition of Na_2CO_3 or of NaOH to the fluid was sufficient to alter its ferment action. In view of these facts it seems advisable, for the present at least, to consider these tests from a qualitative rather than from a quantitive point of view. Nevertheless the difference in lipase is so great that we seem justified in concluding that in infants of this age there is a marked normal variation in its activity.

Amylase was tested for in nineteen cases and found in every instance. It was present in larger quantity than in the cases of group *a*, and in several instances completely reduced the starch solution. Some cases could not be tested for amylase on account of the admixture of saliva to the fluid. However, that saliva did not account for the amylolytic reaction is proved by the fact that in numerous instances the stomach contents failed to reduce starch, whereas the duodenal fluid possessed this activity, and by two instances in which the secretion of saliva was once more inhibited by a local application of alum.

c. Tests On Older Infants.—The group of older infants comprises twenty tests carried out on fourteen infants, varying in age from two weeks to one year. As we had already determined that all the ferments are present in very young infants, these examinations were studied with the purpose of ascertaining possible quantitative differences in the amount of juice obtained, or in the potency of the ferments, compared to that of infants during the first week of life, or of defining a relationship between the composition of the food and the secretion of the three ferments. These infants were of about normal weight; we could not, however, be certain in many cases that they had not at a previous time suffered from intestinal disturbances. Two were nursing babies, the others fed in most instances with a mixture of milk, containing approximately 2 per cent. fat, 6 per cent. sugar and 2 per cent. protein. This group should have included a large number of healthy breast-fed babies, but it was not possible for us to obtain many normal nurslings for this examination, so

23. In giving figures of the amounts of the ferments we realize that they do not represent a quantitative estimation of the ferments but merely denote its activity.

that an extension of this test had to be deferred. As was to be expected, a far greater quantity of duodenal juice was obtained in this group of cases. However, although the difference in this respect was marked between infants of one week and one month, it was slight between those of a month or two and those of five or six months. It should be borne in mind that the total secretion for twenty-four hours was never collected, as this was not practicable.[24]

It was found that whereas infants during the first week of life secreted about 2 c.c. of duodenal fluid in the course of a test of a half hour, infants a month or two old secreted 4 to 5 c.c. On surveying the results of the tests of infants of this group, it seems as if we can make only broad quantitative deductions. Trypsin, it will be remembered, was present to a marked degree in younger infants, as was lipase, and it is only in the case of amylase that we can state that an enzyme was present in older infants in increased amount. For, whereas in the cases under group *b* the glucose formed by the amylase was never sufficient to entirely reduce the 10 c.c. of Fehling's solution used for the test, in these older infants, frequently half of the incubated fluid was able to effect this result. The most marked amylolytic action was obtained with the fluid from an eleven-weeks-old breast-fed infant, in which case 12.7 c.c., that is about a quarter, of the test fluid completely reduced the Fehling's solution. These results have a clinical bearing which will be discussed below.

It has been asserted by some,[25] but denied by others, that the pancreas has a selective activity; that when the food contains a great deal of fat, for example, a lipase of proportionately marked lipolytic power is secreted, and so with the other ferments. Judging from our experiments this would not seem to be the case, for a baby fed on skimmed milk had a lipase equivalent of 3.0 c.c., two fed on milk with 3 per cent. fat had a lipase titrating at 2.2 c.c. and at 2.4 c.c., and still others being fed on milk containing 2 per cent. fat had a lipase varying from 0.9 c.c. to 6 c.c. Nor could a parallelism in this respect be drawn from the results of the protein and starch content of the food, and the respective amounts of trypsin or amylase in the duodenal fluid. Indeed, if the relationship exists, we should expect the nursing infant to have no amylase whatsoever, or at least a marked deficiency compared to an infant receiving a decoction of cereal. On the contrary, the amylase of the two nursing babies was quite as active as that of infants taking milk and barley water, which, from a clinical point of view, would argue strongly against absolute specificity in the secretion of the pancreatic cells.

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24. Recently we have devised a catheter which is self-retaining and with its aid we hope to be able to overcome this difficulty and to collect the secretion for long periods.

25. Pavlov, I.: The Work of the Digestive Glands, Ed. 2, 1910, p. 140.

2. Pathologic Cases.—a. Marantic Infants (Atrophy, Decomposition).—It was with especial interest that we tested a number of infants suffering with severe marasmus, for a lack of intestinal ferments, the more particularly as a deficiency of pancreatic ferments has been suggested as the cause of this ailment. A few years ago Wentworth[26] presented the hypothesis that marasmus was due primarily to the fact that the infant received an improper food, resulting in the secretion of an inadequate gastric juice, which in turn failed to stimulate the cells of the duodenum to elaborate normal secretin. As the flow of pancreatic juice is supposed to depend for stimulation on this hormone, an insufficiency of ferments naturally results. This hypothesis was based on finding a diminished amount of secretin in the mucosa of the intestine of the atrophic, compared to the normal, infant.

Unhappily there is little difficulty in finding marantic infants in hospitals; fourteen were tested. Many were greatly wasted, most of them weighed 6 to 7 pounds, although 2 to 6 months old. It was soon evident that these infants had pancreatic juice containing enzymes of no mean activity. The lipase frequently titrated at 2 to 3 c.c., the amylase converted sufficient starch solution to completely reduce the Fehling's solution, and the trypsin digested the gelatin within twenty-four hours. This was not the exception, but rather the rule. Nor can we fall back on the assumption that the total quantity of pancreatic juice was deficient, for it was fully as copious as in the former group of cases. Indeed in marked marasmus we occasionally meet with a most interesting form of pancreatic hypersecretion, quite different from the cases associated with gastric hypersecretion which will be considered below, a form which may be termed "paralytic hypersecretion." In these cases, there is an almost continuous flow of alkaline duodenal fluid, containing all three pancreatic ferments. The following two instances are typical:

Case 1.—W. E., 3 months old. Marasmus. Weight 6¾ pounds. Receives 2 ounces of milk every two and one-half hours containing approximately 2 per cent. fat, 6 per cent. sugar, 1 per cent. protein.

Oct. 30, 1911. Catheter passed one and one-half hours after feeding; stomach almost empty; contains a small amount of neutral fluid. Pylorus readily traversed. In three-fourths hour 12 c.c. of fluid was aspirated; in one hour 20 c.c. This fluid was obtained while the end of the catheter was about 5 cm. below the pylorus. It was yellow, viscid, alkaline. The secretion was noted as the most constant and profuse yet obtained. When the test was discontinued after one and one-half hours, the secretion seemed somewhat less marked. At this time a test of the stomach contents, which were very scanty, gave a neutral reaction. The infant died four days later. This fluid was 0.2 acid to 1/20 N. NaOH. It contained no lipase, amylase 50, and digested gelatin within twelve hours.

26. Wentworth, A.: Jour. Am. Med. Assn., July 20, 1907, p. 204.

CASE 2.—Dec. 11, 1911. J. C. 5½ months old. Weight 6⅔ pounds. Fed every three hours, 4 ounces of a mixture containing 13 ounces whole milk, 11 ounces water, 1 ounce dextrin malt preparation.

Test two and one-half hours after feeding.

2:25, about 2 ounces of food evacuated from stomach; gas, foul odor.

2:30, catheter passed into duodenum.

2:40, 10 c.c. of alkaline, somewhat cloudy, yellow fluid aspirated.

2:55, 8 c.c. more fluid obtained.

3.00, 6 c.c. watery, neutral yellow fluid.

3:07, 3 c.c. slightly alkaline, faintly bile-colored fluid.

3:12, 2 c.c. darker, thicker, more alkaline fluid.

3:18, 3 c.c. neutral fluid.

3:27, 6 c.c. yellow, slightly alkaline fluid.

3:35, 2 c.c. alkaline, cloudy fluid.

3:40, 2 c.c. more fluid.

3:45, Catheter withdrawn. In seventy-five minutes 45 to 50 c.c. of duodenal fluid was aspirated. The amount of secretion in this wasted infant equaled that of the normal adult.

A previous test three days before had shown a similar but somewhat less marked secretion. At that time the fluid tested as follows: 0.3 acid to 1/20 N. NaOH, lipase 0.9 c.c., amylase 33.5 c.c., gelatin digested in twenty-four hours. The fluid obtained at the second test was 0.1 acid, gave a reaction of 0.7 c.c. to lipase, of 29.3 c.c. for amylase, and digested the gelatin in twenty-four hours.

Here are two instances of a hypersecretion of pancreatic juice in markedly marantic infants, where the normal stimulus of hydrochloric acid was absent or greatly diminished. We have termed this condition paralytic succorrhea or hypersecretion because it seemed to resemble the paralytic secretion of the salivary glands which Claude Bernard[27] was able to incite by dividing the chorda tympani nerve. In dogs an anomaly of secretion similar to that which we have described has been observed, as the result of a diseased condition of the pancreas—continuous watery pancreatic secretion similar to a transudate.[28] In these animals changes denoting exhaustion were found in the glandular acini; it would be interesting to compare this condition with the microscopic picture of the pancreas in a case of "paralytic hypersecretion" in an infant.

b. Pylorospasm Associated with Gastric Hypersecretion.—We have made a separate grouping of the cases of pylorospasm because generally they are associated with an abnormality of secretion, the secretion of gastric juice. Clinically they are frequently included in the general classification of marasmus, a name used to cover a great variety of conditions. However, in most marantic infants hydrochloric acid is deficient, whereas in these cases it is increased, and we have a status which closely resembles simple starvation, brought about by an insufficient quantity of food entering the intestine. In the ordinary case of marasmus, on the contrary, enough food reaches the intestine, but is not utilized as there is some disturbance of absorption or of assimilation. So that

27. Luciani, L.: Physiologie d. Menschen, 1906, ii, p. 62.
28. Luciani, L.: Physiologie d. Menschen, 1906, ii, 75.

from a metabolic point of view the two groups of cases are quite different, although they are characterized by the same chronic atrophic condition. As might be expected, the increased secretion of hydrochloric acid stimulates an increased flow of pancreatic juice, and we find a duodenal or pancreatic succorrhea. This may be termed "functional pancreatic hypersecretion." A study of the duodenal juice of seven cases of this type shows that the secretion is rarely as profuse as in paralytic hypersecretion, and that it differs from these markedly in character. It is not thin and watery, but contains an average amount of lipase and other ferments, and is exceptional merely in being profuse. In one instance it was clear that for some time a hypersecretion of gastric juice stimulated a hypersecretion of pancreatic juice; this stage was followed by one characterized by a marked diminution of gastric secretion, and "functional pancreatic hypersecretion" gave way to a succorrhea of the paralytic type.

3. Chemical and Physiological Observations on the Duodenal Secretion.—In the course of the many tests in the clinic and in the laboratory, we had opportunity to make interesting observations concerning the secretion of pancreatic juice and the properties of the juice itself. It was found that the pancreatic juice generally began to be excreted a few minutes after milk was given, and that it was likewise stimulated by introducing water or a 0.5 per cent. hydrochloric acid solution into the duodenum. These methods were not frequently resorted to in order to obtain the juice as they vitiated the tests. The examinations were almost always undertaken two to three hours after feeding for earlier tests introduced the error of food contamination, and later tests were found to yield a scanty amount of fluid. The mechanical irritation of the duodenum had no effect in inducing pancreatic secretion, nor was secretion stimulated by the infants sucking the catheter or a nipple. Generally pancreatic juice and bile are excreted simultaneously, the amount of bile varying, so that the color of the fluid may be a light or a golden yellow. At times in some cases, and repeatedly in others, pancreatic juice was obtained free from bile; in one case in the course of several tests bile was obtained only once. The duodenal fluid was neutral, alkaline or acid; when acid it was not saved for examination. It is commonly stated that the reaction of the duodenum is alkaline; this, however, was not found to be the case, for the reaction depends entirely on the resultant of the interaction of the alkaline pancreatic and intestinal fluids, with the acid gastric secretion. They may neutralize each other; there is frequently an excess of acid; the reaction is rarely alkaline except in the fasting period. As has been noted in animals, the fluid increases in alkalinity as it flows. When the juice is acid it is turbid, when alkaline, or when rendered alkaline by means of NaOH, it becomes clear. It was noted also that a slight degree of acidity did not markedly inhibit the action of

lipase, but that an increase in alkalinity did retard its enzyme action. In the case of trypsin, on the contrary, a slight acid reaction of the fluid almost nullified the proteolytic activity.

CONCLUSIONS

Whatever progress this investigation is able to offer is due to the introduction of a new method. Heretofore we have had to content ourselves with a study of the pancreas after death or of the stools during life, to gain an insight into the activity of the pancreatic ferments. With the aid of the duodenal catheter, which was devised for the diagnosis and treatment of pyloric obstruction, the opportunity presents itself for the first time of making a direct test of the duodenum in infancy, a test similar to that which is employed in investigating the secretions of the stomach.

By this means fluid was aspirated from infants varying in age from a few hours to a year, some normal, some ailing and was examined for amylase, lipase and for trypsin.

A considerable number of new-born infants were tested before they had been put to the breast. It is of physiologic rather than of clinical interest to note that without the stimulus of food to incite secretion, the three pancreatic ferments were found in the intestine.

During the first week of life the amount of the pancreatic secretion is still very scanty, but it contains the starch splitting enzyme with increased regularity.

In older infants, a month or more of age, there is both an increase in the quantity of pancreatic juice, and a decided augmentation of its amylolytic power. This is a most remarkable functional activity, and one difficult of biologic explanation; for to what purpose is the starch-splitting ferment adapted at this age? It would seem as if the infant was furnished with enzymes competent to digest not only its natural food, mother's milk, but also artificial food. This amylase has the power of digesting a 1 per cent. starch solution, or, for example, barley water, and therefore bears out the old contention of Jacobi[29] and of Heubner[30] that food containing starch can be utilized by the infant in the first month of life.

It seems unwise at present to draw conclusions of an absolute quantitative nature from the tests of ferments; however, we were unable to demonstrate a selective activity of the pancreatic juice — such as an increased strength of amylase when barley water was mixed with the milk, or of lipase when the percentage of fat was increased. The secretion of a large amount of amylase by the nursing baby would also argue against absolute specificity in this regard.

29. Jacobi, A.: Gerhardt's Handbuch, etc., 1876, i.
30. Heubner, O.: Berl. klin. Wchnschr., 1895, p. 201.

Some sick infants were tested. It was soon evident, in a study of marasmus, that the hypothesis is untenable, which suggests that this disease is associated with or is caused by a deficiency of these ferments. Even in advanced cases they were not lacking. It would seem probable, therefore, that absorption is not essentially defective, for the pancreatic enzymes are concerned mainly with the preparation of food for absorption, but that the essence of this disturbance is one of retention and assimilation.

Some of these atrophic infants, although secreting little gastric juice to act as a stimulus, secreted a very large amount of thin, watery juice, containing all the pancreatic ferments, although weak in lipase. This pathologic condition we have termed "paralytic hypersecretion or succorrhea," as it suggested the hypersecretion following the severing of the chorda tympani nerve. The loss of alkali due to the outpouring of this secretion, which serves no end, as it does not neutralize acid, may constitute an important loss to the body, and seems worthy of further study. This is all the more probable when we consider that dogs with pancreatic fistulæ cannot be kept alive for long periods unless they are given alkali.

Cases of pylorospasm associated with gastric hypersecretion furnished numerous examples of pancreatic overactivity of a quite different nature. In these instances the gland probably was overstimulated by the normal agent, the gastric juice. Such cases may be termed "functional pancreatic hypersecretion," and later may develop into the paralytic type.

It gives me pleasure to acknowledge my indebtedness to Dr. Chapin of the Post Graduate Hospital, for the privilege accorded me of carrying out a large part of this work in his wards, and to thank Miss Eleanor Fish and Miss Gertrude Fisher for their able assistance.

154 West Seventy-Second Street.

INFANTILE ECZEMA AND INDIGESTION

PRELIMINARY CLINICAL STUDY WITH ILLUSTRATIVE CASES *

HARVEY P. TOWLE, M.D. AND FRITZ B. TALBOT, M.D.
BOSTON

About two years ago in comparing some then recent clinical experiences, we were struck by the apparent frequency with which the eruption of infantile eczema was associated with a disturbed digestion in a series of cases. From the dermatologic point of view this association was so common as even to suggest at first thought that the digestive disturbance was always present. Reflection soon showed the fallacy of the idea, as, however frequently this double condition might be encountered by the dermatologist, the pediatrist's experience proved beyond question that there are many more children without eczema than with it, even in the presence of pronounced digestive disturbances. The conclusion is unavoidable that the digestive disturbance, even in the eczematous individual, must be regarded merely as an intermediate or contributing factor in the production of the cutaneous manifestations. This preliminary report of our investigations, which is offered for your discussion, deals then with but that small phase of the general problem of infantile eczema which concerns itself with the limited number of cases in which indigestion was actually accompanied by eczematous inflammation.

Three broad questions presented themselves for study in connection with this limited group: (1) type of eruption; (2) character of the concomitant digestive disturbances; (3) frequency with which a definite type of eruption could be demonstrated to occur in connection with a definite form of indigestion.

The first step was naturally to gather all the facts which each case showed as regarded both the cutaneous and the digestive conditions.

The second step was to scrutinize the combined records in a general way, first from a dermatologic and then from a pediatric point of view in order to determine whether the general conclusions justified a further, more detailed study of the subject.

Having decided that the cutaneous and digestive conditions were more or less definitely constant, there remained only the task of deter-

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*From the departments for the skin and for children, Massachusetts General Hospital, Boston.

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mining by a detailed analysis of the data whether a definite type of eruption was always associated with a definite form of indigestion.

We propose to offer the facts for your consideration in this same order, presenting first the general review from both the dermatologic and the pediatric points of view and then the detailed considerations of both.

THE ERUPTIONS — GENERAL REVIEW OF DATA

The method of obtaining clinical facts is so ordinary and familiar as to need no description. We may therefore state without further detail that the skin records seem to lead to the general conclusion that the eruptions of infantile eczema might be divided with a fair degree of definiteness into two groups. Occasionally, however, a case was seen which presented characteristics belonging to both and which might therefore be considered as intermediate. The dominant features which differentiated the eruptions of the first group (to which we will hereafter refer as Group I) from the second (Group II) were the greater acuteness and intensity of the inflammatory process and its more pronounced tendency to exudation. A more detailed account of these two eruptive types will be given further on.

THE DIGESTION — GENERAL CONSIDERATIONS

Next comes a similar preliminary analysis from the pediatric point of view.

The facts concerning the state of the digestion have been collected through the analyses of the stools which one of us (F. B. T.) has made. As this method of stool examination in connection with the study of the digestive processes in infants has been developed but recently, a brief description may be necessary to a proper appreciation of the value of conclusions based on information obtained in this manner. To the disturbances of digestion an etiologic connection with the production of eczema in infants has been attributed many times before, but the coarser methods of investigation, which alone have been available hitherto, have invariably failed, in the absence of clinical symptoms, to furnish the necessary proof.

The recent advances in our knowledge of the physiology and pathology of infant digestion, however, have thrown much light on many formerly obscure conditions. Consequently, in the diagnosis and treatment of the diseases of the infantile digestive tract, the pediatrist now considers the examination of the stools as important a routine measure as auscultation in diseases of the lungs or urinalysis in affections of the kidneys. For example, in the presence of a disease of the lungs we cannot make an accurate diagnosis from the clinical symptom of cough alone. In the indigestions of infants the clinical symptoms do not tell whether they

are due to the fats, to the carbohydrates or to the proteins. In the first instance, we can obtain by auscultation an accurate idea of the conditions in the lungs which have produced the cough. In the same way the examination of the stools yields to the pediatrist accurate information concerning the process of digestion in the infant. Through the facts gathered from many previous investigations and experiments he can interpret with fair accuracy from the results of the stool analysis whether the indigestion is due to the fats, the carbohydrates or the proteins, and can then regulate his treatment accordingly.

Two methods are used in the examination of the stools — the macroscopic and the microscopic — which supplement each other. The technic of the microscopic method and, most of all, its accurate interpretation, demand such extensive and specialized experience that we cannot at this time enter on its detailed description. The macroscopic method, however, is so much more easily learned that a brief summary of the macroscopic features presented by the stools in the different disorders of the infantile digestion may be of value in connection with this report.

Through the more intimate data collected by the microscope used in conjunction with the grosser method of macroscopic inspection, it is now possible to differentiate with greater accuracy than before the form of the indigestion by the macroscopic appearances presented by the stool.

The most common fat stool is soft and contains in varying abundance soft curds which have been found to be composed of fat in the form of fatty acids or soaps. These curds look like small particles of undigested milk imbedded in a mucus which is usually more or less greenish. The "soap stool," a second form of fat indigestion, is of a light yellow or whitish color, has a shiny surface, a soapy appearance and is almost entirely composed of fat. There is a third but less common type of stool, almost wholly composed of fatty acids, which presents the appearance of Indian meal.

An acid, burning stool is an indication that the starches, which under normal conditions are converted into sugar and in this form absorbed, have, owing to a faulty digestion, undergone a further reduction by which the sugar has been broken up into lactic, acetic or succinic acids. If an acid stool is stained with Gram's or Lugol's solution the starch granules present are stained blue.

In the case of lactalbumin and whey, protein indigestion gives no clinical signs in the stools; but the presence of tough, bean-like curds indicates that casein digestion is disturbed.

The macroscopic examination, however, does not help us to determine the relative amount of fats contained in the stool nor does it reveal the presence of small amounts of starch. This information can only be

obtained by the microchemic examination. The microscope must also be used to detect the content of meat fibers, cellulose and vegetable detritus.[1]

The fundamental principles so sketchily described above were applied to the analysis of the information afforded by such macroscopic and microchemic examinations of the stools.

TYPES OF INDIGESTION IN ECZEMA

A general survey of the data seemed to indicate that there were two types of indigestion associated with infantile eczema; one, a variety of fat or carbohydrate indigestion; the second, a grosser form of which the chief evidence found in the stools was the presence of undigested particles of solid foodstuffs.

In order to determine if the conclusion, drawn from the facts relating to the question whether infantile eczema manifests itself in two eruptive forms, has any significance in view of the second conclusion, drawn from the statement that two forms of indigestion were encountered in infants with eczema, we must make a detailed analysis of the data on which these general conclusions were based. The final conclusion will be contained in the answer to the question: "Is the relationship limited to a definite form of eruption with a definite type of indigestion?" Or, to put the question in another way, "Can it be demonstrated that a given type of eruption is associated sufficiently often with a definite form of indigestion to render the conclusion probable that their association is not mere accident?" The answers to these questions must be found in the observations recorded above, testing the conclusions to which the dermatologic records would lead the student by the conclusions apparently indicated by the facts recorded by the pediatrist.

As the most graphic method of presenting the facts, we shall recite the histories of certain selected cases to illustrate the types of eruption which are usually found in association with the various forms of indigestion, as of fats, carbohydrates and the solid foodstuffs.

ERUPTIONS IN GROUP I

Therefore Case 9 is given to illustrate the type of eruption which is usually encountered in the presence of an indigestion of fats.

CASE 9.—The patient, a baby, was originally admitted to the hospital with a vesicular dermatitis which involved nearly the whole head and also a few small areas on the body. He was given a food formula which figured 4 per cent. fat, 7.7 per cent. sugar and 2 per cent. protein. An examination of the stool made seven days before discharge, i. e., one month after admission, showed an excess of fats in the form of soaps. Although this indicated that the infant was being given more fat than he could digest, the formula was not changed at this time. When discharged from the hospital the skin was seemingly about well.

1. A detailed description for those interested in the technic of the microchemic examination will be found in the Archives of Pediatrics, February, 1911, xxviii.

Three days later he was readmitted to the hospital with a recurrent vesicular eruption which this time was limited to the cheeks, forehead and chin. He was again given the same food formula as when in the hospital before of 4 per cent. fat, 7 per cent. sugar and 2 per cent. protein. The conditions in the skin improved, according to the record made on the tenth day after readmission. On the other hand, the examination of the stool, under the same date, recorded that the stool contained a large excess of fats, was pale yellow, greasy and sour.

It is interesting to note that the next record of the cutaneous condition, made five days after this stool examination which showed the increase in the excess of fats, states that the face had been growing worse.

Now, without altering the external treatment, the fat content of the food was reduced from 4 per cent. to 2 per cent. without other change than the addition of lime-water. This reduction in the amount of fat was promptly reflected in the findings from the stool analysis, for the very next day only a slight excess of fat was found.

In view of the fact that no change had been made in the external treatment, the note made five days later is espeecially suggestive: "The condition of the skin has improved much since the reduction of the fat in the diet."

Aside from the intolerance of fat, this case pictures well the sort of skin manifestations which have usually been found in association with a fat indigestion. The cutaneous symptoms gave evidence of an acute inflammatory process with a marked exudative tendency; that is, the eruption was of the type described in Group I. The case also illustrates the seat and the characteristic spread of this type. Attention must also be called to the suggestively significant appearance of undigested fat in the stools several days before the cutbreak of the eruption.

Although such acute exudative inflammations of the skin as this were found, in the majority of instances, to be associated with an indigestion of fats, similar inflammations were occasionally seen in cases in which the dominating feature in the stools was not fatty excess, but undigested starch. As an illustration, Case 17 may be cited.

CASE 17.—The patient was a child of 16 months whose eczema was said to have existed since he was 6 weeks old. Since birth he had received at intervals, whose length and frequency apparently depended on his spells of crying, varying amounts of condensed milk, a food low in its fat content and high in its sugar. In addition to condensed milk he was now receiving from the common table such foodstuffs as pudding, a little rice or potato and bread and butter.

On October 14 the stool showed no free fat or fatty acids and only a slight amount of soaps, but did show, both macroscopically and microscopically, a large amount of starch. As to the skin, the record says that the face "was almost universally swollen and reddened and covered with vesicles ruptured and oozing and crusted and, to a lesser degree, the arms." "Itching was intense."

Although the mother was given definite directions concerning the diet they were only partially carried out. Still, even this partial modification of the diet was followed by an improvement in the cutaneous disturbances and, in the stools, by the total disappearance of the slight excess of soaps previously noted and by the reduction of the amount of starch from large to slight.

In connection with the inflammation of the skin it was noticeable that the "improvement" recorded consisted not in the disappearance of the eruption, but in the modification of its intensity. Whereas the skin manifestations were formerly of a moderately acute, exudative type, the intensity of the inflammatory

process was now greatly lessened. The eruption no longer showed exudative lesions but dry, infiltrated, profusely scaling areas situated on the body. The itching, which was once so intense as to interfere with sleep, also decreased and was no longer troublesome.

From the dermatologic point of view the interesting feature in this case is the behavior of the eruption. With the indigestion of fat present, the cutaneous symptoms were those of Group I which, coincidently with the elimination of the fat indigestion, declined to the type of Group II notwithstanding the persistence of a small amount of starch in the stools.

From the pediatric point of view attention is attracted to the disappearance of the clinical symptoms of indigestion which followed the reduction of the amount of starch in the food and to the gain in weight and improvement in the general appearance of the patient.

Case 31 was exceedingly interesting because of the seemingly close connection between the disturbances in the skin and the disturbances of the digestion. So parallel were the fluctuations of the eruption to the changes in the digestion that the suggestion of their relationship was unavoidable.

CASE 31.—When first seen the child was 5 months old and showed no particular disturbance of the skin. He was undersized and was reported to have a poor digestion and to have gained nothing in weight in the last three weeks. His food formula showed that he had been receiving 5 per cent. of fat, 6 per cent. sugar and 1.5 per cent. protein. There were present symptoms indicative of a chronic intestinal indigestion due to fat. The formula was accordingly changed to fat 2 per cent., sugar 7 per cent. and protein 1.65 per cent.

This increase in the amount of sugar from 6 per cent. to 7 per cent. was followed immediately by marked symptoms of sugar indigestion and two or three days later by an eruption on the skin.

A reduction of the percentage of sugar from 7 per cent. to 5 per cent. gave relief from the symptoms of the indigestion of sugar. The fat indigestion was not affected. The digestive balance, however, was now so delicate that slight changes in the formula sufficed to induce a return of the clinical symptoms of indigestion.

Coincidently with the appearance of the symptoms of sugar digestion which followed the increase in the percentage of sugar in the diet, the skin showed disturbances due to an acute, exudative, inflammatory process which were extensively distributed over the body, extremities and head, but which it must be noted were equally as intense on the body as on the head, although the eruption was everywhere exudative.

The intensity of the cutaneous manifestations declined as the conditions due to the indigestion of sugar improved but nevertheless persisted, as did the indigestion of fat. Thereafter, however, the cutaneous reactions were so sensitive that the slightest dietary indiscretion was followed almost immediately by an increase in the intensity of the symptoms in the skin. The interest in this lies in the coincident increase in the delicacy of the digestive balance, already mentioned.

ERUPTIONS IN GROUP II

Contrasted with these acute inflammatory disturbances of the skin in which the exudative tendency was a prominent feature and in which the associated digestive disturbance was usually due to fat, were the

eruptions in which the picture in the stools of an indigestion of fats and starches was subordinate to the symptoms of an indigestion due to more solid foodstuffs. These digestive disturbances of Group II were usually accompanied by a cutaneous eruption of moderate or mild intensity which lacked the tendency to exudation described above (Group I) and, in several other particulars which will be referred to again, differed from the symptoms of the cases in Group I. Nevertheless, we can advance no proofs as to the etiology of Group II as the changes in the digestive processes do not manifest themselves in the stools in any definite manner. For the present, then, we must abandon the cases in this group, leaving to the future the discussion of such questions as the meaning of the greater intensity of the skin reaction when associated with fat intolerance.

Scrutinizing the facts summarized above, the impression given is that whereas the exudative inflammatory processes for the relief of which the patient sought the dermatologic clinic showed a constant, though perhaps not absolute, association with the disturbances of digestion due to fat and occasionally to the carbohydrates, but rarely to any other forms of indigestion; the non-exudative cases of Group II were rarely associated with the dominance of the stool picture by fats. Oftentimes, indeed, the stools contained neither fats nor carbohydrates in abnormal amounts. In other words, the indigestion of fats and carbohydrates was an exceedingly frequent accompaniment of the exudative inflammations of the skin in contrast to the results of the stool examinations in the cases of Group II.

NATURE OF EXUDATIVE ERUPTION

These indications obviously pointed to a more careful study of the acute, exudative inflammatory process as the next step. Briefly stated, the following were the important facts revealed:

The general aspect and composition of the eruption were the same as that which we commonly associate with vesicular eczema and was therefore not characteristic.

The course of the inflammatory process and the evolution of the lesions also corresponded to the familiar course and evolution of vesicular eczema.

The prodromal symptom of pruritus preceded the eruption by an interval the length of which varied within wide limits in the different individuals.

The onset of the eruption varied from acute to moderately acute.

The primary seat was, almost without exception, on some portion of the head, ordinarily the cheeks, less frequently on the forehead or scalp and occasionally on two or more of these regions nearly, if not quite, simultaneously.

It was the tendency of the exudative eruption to remain limited to the regions of the head for an appreciable length of time, even for months. Many cases, in fact, showed no tendency to spread to other parts.

When the eruption did appear elsewhere than on the head, its spread was from above downward, invading one part after another in orderly succession.

However great and extensive the spread, the most intense manifestations always appeared on the cheeks and, in a slightly lesser degree, on the forehead and scalp.

The eruptions which appeared on other regions than those of the head were most often encountered on the lower portions of the abdomen, the sides of the chest and on the buttocks, all of which regions are notably exposed to external traumas. The chin was affected in less than 10 per cent. of the cases and the upper and lower extremities even less frequently.

The eruption on the face was symmetrically distributed. The lesions were usually abundant and discrete for a variable length of time, but eventually coalescing over the flush areas of the cheeks, where they were always in the greatest abundance, to form oval placards of considerable size. The cheeks not covered by the large patches bore discrete lesions whose numbers decreased as the distance from the main seat increased. Even in the most severe cases a zone of skin free from all eruptive manifestations completely surrounded the lesions on the cheeks.

The eruption appeared occasionally on the auricles of the ears, but never by direct extension of the process from the cheeks.

On the forehead, the inflammatory process, when fully developed, manifested itself in the form of a broader or narrower band which occupied the middle portion of the forehead. The process never extended quite to the hair line or to the brows, and rarely appeared between the brows.

The eruption on the scalp was usually not abundant but consisted of a few scattered, roundish patches which were most often seated on the lower parts of the sides of the head.

The eruption on the scalp was usually not abundant but consisted of eczema recently described so comprehensively by Brocq. It occurred there in round, moderately well-defined patches, in moderate abundance. In an occasional case the patches were present in greater numbers and, by confluence, even covered considerable areas.

The form of eruption was the same on the lower abdomen and the extremities as on the chest except that, on the abdomen, it showed a greater tendency to confluence and, on the wrists, a greater intensity, as was manifest by the more numerous papulovesicles, their brighter color and sharper definition.

Itching was a usual accompaniment of the eruption, but was less intense in most "acute" cases than in the subacute or subchronic cases of Group II. The fact was noteworthy that, as the eruption improved, the itching and the feeling of irritation increased.

The cutaneous reaction was increased over the body surface generally regardless of the presence or absence of eruptive manifestations.

The course of the cutaneous symptoms was marked by the same irregular fluctuations in intensity as are met with in ordinary eczema.

IRREGULARITY OF NON-EXUDATIVE ERUPTIONS

If the symptoms of the subacute or subchronic eruptions of Group II are compared with the eruptions of Group I, just described, it will readily be seen that in no particular do they exhibit the same constancy or regularity.

In general aspect, the eruption resembled that of a papular or a papulovesicular eczema of mild intensity with little tendency to exudation.

The course, although fluctuating, exhibited less pronounced changes.

The prodromes and the onset were much the same as in the acuter type.

The primary seat of the eruption was not at all constant. Except that the eruption usually made its first appearance on some part of the trunk or extremities, nothing characteristic was discovered.

The eruption was not infrequently unilateral and limited to a single part.

The character of the spread was irregular and disorderly.

The general cutaneous irritability was less disturbed.

The eruption usually manifested itself in the form of more or less abundant patches, irregularly and often unilaterally distributed and varying greatly in size. They were ill-defined, but slightly infiltrated, pale red, exfoliating abundantly and covered by a larger or smaller number of pale red, fine, acuminate papules. In the immediate neighborhood, widely separated, discrete papules were to be seen. Occasionally a few papules showed small vesicles on their summits. Occasionally also one or two patches were distinguished by a more marked tendency to exudation than their fellows and developed a considerable number of discrete papulovesicles. Such appearances, however, were not characteristic of this type and were but transitory and occasional conditions.

SUMMARY

Definite conclusions are, of course, not possible from this incomplete study of the etiologic relationship of indigestion to infantile eczema. Tentative conclusions may perhaps be allowed. In such fashion it is suggested that:

1. The acutely inflammatory form of eruption in infantile eczema presents so many features which are constant in occurrence and in form that its claim for consideration as a definite, fixed type of disease deserves further attention.

2. For directly opposite reasons, the less intense inflammatory form of eruption cannot lay claim to such consideration.

3. The stool findings show that the indigestion of fats and of carbohydrates are the only types which can be demonstrated to occur with any regularity and definiteness in association with infantile eczema.

4. The occurrence of the acute exudate type of eczematous inflammation of the skin in such frequent association with an indigestion of fats and sugar indicates that the process in the skin and the process in the digestive tract probably have some etiologic relationship.

5. Contrariwise, the fact noted at the outset that the majority of infants presenting the same symptoms of indigestion described above do not likewise present a cutaneous reaction points to the inevitable conclusion that some underlying condition, probably systemic, which the eczematous infants possess, is lacking in the non-eczematous individuals.

6. Therefore, indigestion must occupy an intermediate position, if any, in the mechanism of the production of eczema.

453 Marlboro Street—311 Beacon Street.

INTESTINAL TOXEMIA IN THE NEW-BORN*

JOHN LOVETT MORSE, A.M., M.D.

Associate Professor of Pediatrics, Harvard Medical School; Associate Visiting Physician, Children's Hospital, and Infants' Hospital

BOSTON

The condition of which I shall speak as intestinal toxemia of the new-born is, I am inclined to think, not at all an uncommon one. All who have much to do with the new-born infant must be more or less familiar with it. The text-books, however, either do not refer to it at all or so casually that the reference is very likely to be overlooked. This is probably because the writers have considered it too simple a matter to describe or because they have described it under other names or in connection with other diseases. The majority of the cases of what I have considered to be examples of this condition which I have seen in consultation have, however, been mistaken for other diseases.

I shall base my description of the symptomatology of this condition on the cases which have recovered, as none of the babies which have died of what I have supposed to be intestinal toxemia have been autopsied.

SYMPTOMATOLOGY

A baby that was normal at birth and has continued to seem normal and to do well up to the second, third, fourth or even fifth day, becomes rather suddenly ill. He is likely to cry and moan considerably, although he is not infrequently unusually quiet. Attacks of cyanosis are a common and early symptom. Twitching of the extremities, slight general rigidity and retraction of the head come on in many instances, while convulsions are not infrequent. The temperature is, as a rule, only moderately raised, but may be high. In the more severe cases the baby refuses to nurse. Vomiting is uncommon. There is in most instances no diarrhea; in fact, the tendency is to constipation. In the majority of instances the symptoms develop before the baby has ceased to pass meconium and it is very common to find that it has not passed as much as the average baby. If the stools are not composed of meconium, they are usually small in amount, loose, dark-brown and contain small, soft curds and mucus. They are often offensive. The abdomen may be distended, but usually is not. Loss of weight is generally rapid, the face becomes pinched and in all but the mildest cases it is evident that the baby is seriously ill. If the

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bowels are thoroughly cleaned out, all food stopped for a time and water given freely, recovery is usually rapid and complete. If the bowels are not cleaned out and food is continued, a fatal termination is not uncommon and recovery is, in any event, slow.

CASE REPORTS

The following case histories illustrate the symptomatology of the condition:

CASE 1.—Henry H. was born at 1 a. m., January 25, after an easy, low forceps delivery. He was normal at birth and weighed 8¾ pounds. He passed both urine and meconium immediately after birth. He was put to the breast at the ordinary intervals after twelve hours, but apparently obtained very little. He seemed all right, except that he cried considerably, until the morning of January 26, when he became very fussy and his temperature was found to be 102 F. The bowels moved during the afternoon, the movements consisting of meconium. He was given two feedings of 1 ounce each of a mixture containing 1.50 per cent. of fat, 4 per cent. of milk sugar, 0.25 per cent. of casein and 0.25 per cent. of whey proteins. He became a little quieter after this, but his temperature at 6 p. m. was 103.5 F. He was seen in consultation at 9 p. m., January 26.

He was well developed and nourished and of good color. Nothing whatever abnormal was found on a careful physical examination. A movement, which was seen, consisted entirely of meconium.

He was given a teaspoonful of castor oil, all food was stopped and water was given freely. The bowels moved several times during the night and the temperature the next morning was 99.5 F. He was then fed again, partly on the breast and partly on the bottle, but there was no recurrence of the symptoms.

CASE 2.—Helen P. was born at 12 m., July 17, after a moderately severe labor induced two weeks ahead of time because of albuminuria in the mother. She was the second of twins. She weighed 6¾ pounds. She was pale, but cried fairly vigorously. She was quiet during the afternoon, but in the evening began to cry and moan. She had kept this up almost continuously. Usually there was a moan with each breath, but at times she cried hard, as if in pain. She passed urine freely, but did not pass any meconium until the early afternoon of July 18. She had had no food, but had taken a little water. She was seen at 5:30 p. m., July 18.

She was fairly developed and nourished and of good color. The fontanelle was somewhat depressed. The pupils were equal and reacted to light. The mouth and throat showed nothing abnormal. She was able to swallow. The heart and lungs were normal. The abdomen was somewhat distended, but otherwise normal. The lower border of the liver was palpable 3 cm. below the costal border in the nipple line. The spleen was not palpable. The navel was healthy. The extremities were normal. There was no spasm or paralysis. The knee-jerks were equal and normal. There was no Kernig's sign. She moaned with each inspiration and acted as if in pain. The rectal temperature was 100.4 F.; the pulse, 160; the respiration 68.

She was given a suds enema and a teaspoonful of castor oil at once. Water was ordered to be given freely during the night and a weak modified milk the next morning.

Considerable meconium was obtained with the enema and the bowels moved freely during the night. The temperature was normal the next morning and she was perfectly comfortable. She did uninterruptedly well from that time on.

CASE 3.—Granville W. was born October 12, after a very rapid labor, two weeks ahead of time. He was normal at birth and weighed 6 pounds. The breast milk came in on the third day and he took it fairly well.

He had been given special care, but had been dressed and bathed. He seemed to be doing well until the morning of the third day, when he had an attack of cyanosis lasting a minute or two. The pulse went up to 180 during the attack, then dropped to 120. He had several similar attacks during the morning, and at noon the attacks of cyanosis were accompanied by irregular contractions of the face and hands. The head and eyes were always turned to the right. He was given paregoric and bromid and had no attacks for twenty-six hours. They recurred, however, on the morning of the fifth day. The twitching was then most marked in the left side of the face and in the left hand. The temperature had not been above 99.2 F. He was partially cleaned out with sweet oil and magnesia in the beginning. The bowels had not moved very well since then. He had not vomited. He was seen at 4 p. m., October 18.

He was small and thin, but of good color. He opened his eyes, looked about, gaped and acted like a normal baby. The fontanelle was slightly depressed. There was no rigidity of the head or neck. The pupils were equal and reacted to light. There was no spasm or paralysis of any of the muscles controlled by the cranial nerves. The heart, lungs and abdomen were normal. The liver was palpable 2 cm. below the costal border. The spleen was not palpable. The stump of the cord and navel were healthy. There was no spasm or paralysis of the extremities. The knee-jerks were equal and normal, the abdominal and cremasteric reflexes lively. Kernig's sign was absent. The last movement, which was seen, was watery, dark-brown in color, contained many fine curds and was foul in odor.

He was given a teaspoonful of castor oil, the breast milk was stopped and whey, ½ to 1 ounce, every two hours, ordered. After the bowels were cleaned out he had no recurrence of his symptoms and did uninterruptedly well.

CASE 4.—John H. was born at full term, after a normal labor, October 28. He seemed normal at birth and weighed 9¼ pounds. He was put to the breast and took it well. He seemed a little feverish October 30, but the temperature was not taken. The next day he was dusky, and the temperature was found to be 103 F. He breathed with some difficulty, as if there was some obstruction, had clonic motions of the face and rolled his eyes. The temperature from this time on ranged between 103.6 F. and 104.8 F. He had much difficulty in nursing and swallowing, but did not vomit. The movements continued to look like meconium. He began to hold his head backward November 2. He was seen in consultation at 5 p. m., November 2.

He had evidently lost much weight. His face was pinched and he seemed very feeble. The fontanelle was depressed. He was generally somewhat dusky. The lips and skin were dry. The heart, lungs and abdomen were normal. The navel was healthy. The liver was palpable 3 cm. below the costal border in the nipple line. The spleen was not palpable. There was no spasm or paralysis of the extremities. The knee-jerks were equal and normal. Kernig's sign was absent. The pupils were equal and reacted to light. There was no dulness under the manubrium and no tumor was felt in the suprasternal notch. The rectal temperature was 103.8 F.; the pulse, 160; the respiration, 45. The movements which were seen were small, dark-green, sticky and contained a few fine curds.

He was given a teaspoonful of castor oil and diluted breast milk and whiskey. The bowels moved freely, the temperature quickly came down to normal and he made an uninterrupted recovery.

My interpretation of the etiology of these cases is that a bacterial infection of the meconium, through either the mouth or anus, takes place within the first twenty-four or forty-eight hours after birth; that on account of the incomplete evacuation of the intestines the toxic products

formed in the meconium as the result of this infection are absorbed into the circulation and that these toxic products cause the symptoms. Corroborative evidence in favor of this conception is that, as the meconium is made up of protein, the products of bacterial action in it must necessarily be putrefactive in character and, therefore, toxic. It is a well known fact, moreover, that cyanosis may be enterogenous in origin. It may be asked why this symptom-complex is not merely a manifestation of septic infection, that is, of the entrance of bacteria into the circulation. I am unable to say positively that this is not the case, because no blood cultures were made from these patients. The early onset of the symptoms, the absence of any nidus of infection and the absence of other signs of sepsis, such as hemorrhages, marked jaundice and boils, make it improbable, while the rapid and complete recovery after the evacuation of the bowels seems sufficient to exclude it. It may also be asked why it is not simply a manifestation of starvation, analogous to the so-called "inanition fever." The answer is that it occurs both in babies that have not been fed and in those that have been, and that the withdrawal of food in connection with the evacuation of the bowels relieves it.

DIAGNOSIS

The diseases for which this condition is most likely to be mistaken are cerebral hemorrhage as the result of injury at birth, meningitis, hemorrhagic disease of the new-born and septic infection of the new-born. The diagnosis from septic infection of the new-born is the most difficult. The symptoms appear earlier, as a rule, than do those of septic infection and the temperature is usually lower than in sepsis. There is no local nidus of infection, and marked general and local symptoms of infection, such as hemorrhages, deep jaundice and furuncles, are absent. There is a tendency to constipation and the stools are usually meconium-like in character. In many instances it is, however, impossible to make a positive diagnosis without the therapeutic test of free catharsis. Hemorrhagic disease of the new-born can be excluded on the absence of hemorrhages. Meningitis is extremely rare at this age and, when it occurs, it is a part of a general septic infection. There is almost invariably bulging of the anterior fontanelle in meningitis and usually when there is a cerebral hemorrhage. There are usually symptoms of focal irritation in hemorrhage and often blood in the nose and nasopharynx, while in both cerebral hemorrhage and meningitis there is likely to be spasm of the extremities and exaggeration of the knee-jerks. These latter symptoms, as well as other symptoms of cerebral irritation, may, however, also be present in intestinal toxemia. A lumbar puncture will settle the diagnosis at once in a doubtful case.

TREATMENT

The treatment consists in the administration of one or two teaspoonfuls of castor oil, the withdrawal of food for from twelve to twenty-four hours and the feeding of water or water sweetened with saccharin. It is also well to irrigate the bowels in the beginning. Bromid or stimulants, such as strychnin or caffein, may be used, if necessary. The best food, after the period of starvation, is human milk, plain or diluted, according to the individual baby's condition. Next to this, a mixture of cows' milk, low in fat, high in milk sugar and with a moderate amount of proteins, part of these preferably in the form of the whey proteins. It is important to give a high percentage of milk sugar in order to change the bacterial activity from the proteolytic to the fermentative type.

70 Bay State Road.

STUDIES IN METABOLISM OF AMAUROTIC FAMILY IDIOCY *

HENRY HEIMAN, M.D., SAMUEL BOOKMAN, PH.D., AND BURRILL B. CROHN, M.D.
NEW YORK

PART I.—BY HENRY HEIMAN, M.D.

Carefully as this disease has been observed for over a quarter of a century, the obscurity regarding its true nature is still as great as ever. While Sachs'[1] somewhat modified view of its congenital origin has gained many adherents, among these such careful observers as Schaeffer[2] and Vogt,[3] there are a considerable number of authorities who hold the opinion that this affection is acquired in nature. Though few now share the view of Hirsch[4] that some toxic substance plays a rôle in the etiology of the disease, it is on theoretical grounds alone that it has been discarded. Yet this view is not so wholly improbable or unreasonable as not to demand better founded reasons for its final abandonment. Moreover, within recent years certain observations have been recorded which seem to indicate that other organs besides the nervous system are affected in this disease. Thus Brooks[5] has found morbid changes in the pancreas, hypophysis, thymus and adrenals. If toxic agents are at work, and more especially if the organs playing an important rôle in the production of internal secretions are affected, we may expect that the metabolic processes would show some departure from the normal.

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proved by the very thorough recent histologic and pathologic studies of Schaffer, Vogt, Brooks, Sachs and Strauss,[6] and others, it would be interesting to discover in the excretions the chemical evidences of the degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so

*Read at the Meeting of the American Pediatric Society, Hot Springs, Va., May 29, 1912.

1. Sachs: Jour. Nerv. and Ment. Dis., 1887.
2. Schaffer: Jahrb. f. Psychol. u. Neurol., 1907, p. 121; Ztschr. d. Jugend. Schwach., No. 2, p. 75; *ibid* No. 3, p. 19.
3. Vogt: Archiv. f. Kinderh., 1909, li.
4. Hirsch: Jour. Nerv. and Ment. Dis., 1898, p. 538.
5. Brooks: Tr. Assn. Am. Phys., 1911.
6. Sachs and Strauss: Jour. Exper. Med., 1910, xii, 685.

integral a part of nerve tissue, namely, phosphorus and sulphur. Despite the valuable information that could be expected from a chemical study, this aspect of the disease has been, up to the present, almost entirely neglected. A perusal of the recent literature fails to show any extended metabolic studies. The only investigation dealing with the chemical side of amaurotic family idiocy is that of Mott. In a paper detailing the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott[7] shows a very distinct change in the relative proportions of simple and nucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition with an increased water content.

The opportunity having presented itself of observing two cases of this disease, it seemed worth while to undertake the study of its metabolism. As will be seen from the hospital records, both were typical cases of amaurotic family idiocy. The first case was submitted to one period of investigation, the second to two at an interval of twenty-four days.

CASE REPORTS

CASE 1.—The first case, David F., 15 months old, born in the United States, of Russian Jewish parentage, was admitted to the children's service of Dr. Koplik at the Mount Sinai Hospital, April 7, 1911. One other child was well.

Past History.—Full term, breast-fed for twelve months; enterocolitis of two months' duration at 6 months of age; measles at 12 months of age; never sat up nor stood up, nor made any attempt to speak; no history of convulsions. Since the attack of measles three months prior to this report, mother noted gradually increasing drowsiness and weakness. There was no vomiting, no fever, no other disturbances, but marked sweating especially at night. Bowels markedly constipated.

Physical Examination.—General condition fair, well nourished; no rigidity of neck; eyes staring, apparently blind; right pupil larger than left; pupils react sluggishly; heart, lungs, and abdomen negative; spasticity of all four extremities; reflexes not obtained.

April 28, 1911. Fundi show cherry-red colored spot in the center of a white area outside of each disk, which is atrophic and white.

Urine negative.

During the stay in the hospital, the condition of the patient did not change.

CASE 2.—The second case, H. Sch., aged 7 months, born in the United States, of Russian Jewish parentage, was admitted to the hospital Sept. 12, 1911. Family history negative. Four other children well; no miscarriages.

Past History.—Breast-fed up to time of examination. At 14 weeks of age the child had an attack of bronchitis for nine days. Mother dates illness from that time. No other diseases.

Present History.—Since attack three months prior to this report, the mother had noticed that child no longer played, but slept most of the time. Does not take the breast as readily, does not sit up, and can not stand. Child apparently can not hear or see as well as it should. No convulsions; no vomiting. Bowels move twice daily.

Physical Examination.—General condition good; patient well nourished; slightly anemic. Internal strabismus; eyes apparently follow light. Hearing normal. Loud blowing systolic at apex, heard with greatest intensity in third

7. Mott: Arch. Neurol., Path. Lab., London County Asylum, iii, 218.

and fourth interspaces. Lungs negative. Liver palpable two fingers below rib border. Spleen negative. Spasticity of both upper and lower extremities; knee-jerks normal; no ankle clonus. Cherry-red spot present. Noguchi test negative. Urine negative.

Most important in a consideration of the metabolism of such a condition as amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposis present. So good was the general health of the children, that during the periods of observation in both cases a gain of weight was noted. Thus the patient, David F., gained 180 gm.; Patient 1, H. Sch., gained in the four days of the first investigation 80 gm.; in the second period, 30 gm. In all these instances the nourishment was well taken, the diet consisting of milk undiluted in Case 1, and diluted in Case 2. The caloric intake was in excess of the established figures of Heubner (100 calories per kilo per day).

TABLE 1.—INVESTIGATION DURING A FOUR-DAYS PERIOD OF THE DAILY NOURISHMENT OF DAVID F. (CASE 1), AGED 15 MONTHS

	Ounces	Calories
Milk	27	560
Cocoa	9	200
Broth	5	10
		770

Weight 8.4 kilos equals 95 calories per kilo per day.

TABLE 2.—DAILY NOURISHMENT OF SCH. (CASE 2), AGED 7 MONTHS

	Ounces	Calories
Milk	36	730
Maltose	1½	180
		910

Weight 7.65 kilos equals 119.3 calories per kilo per day.

The minute details of this metabolic study will be given in the second part of this paper by Drs. Bookman and Crohn. The general results of the present investigation are shown in the accompanying tables:

TABLE 3.—METABOLISM STUDY; INTAKE, OUTPUT AND DAILY AVERAGES IN AUTHORS' CASES

	N	S	P	Cl
INTAKE				
David F.	5.831	0.5087	0.6997	1.529
Sch. (I)	3.220	0.521	0.393	0.753
Sch. (II)	5.610	1.084	1.115	1.253
URINE				
David F.	2.834	0.23235	0.3553	0.581
Sch. (1)	1.2382	0.1075	0.121	0.3115
Sch. (II)	3.078	0.302	0.255	0.862

	N	S	P	Cl
STOOL				
David F.	0.225	0.0775	0.0496	.....
Sch. (I)	0.2385	0.0424	0.0104	.....
Sch. (II)	0.076	0.084	0.1924	.....
TOTAL OUTPUT				
David F.	3.059	0.3099	0.4040	0.581
Sch. (I)	1.4767	0.1499	0.1313	0.3115
Sch. (II)	3.154	0.388	0.4482	0.862

TABLE 4.—METABOLISM STUDY IN AUTHORS' CASES. DAILY AVERAGES

	N	N %	S	S %	P	P %	Cl	Cl %
RETENTION (PER CENT. OF INTAKE)								
David F.	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948	62.0
Sch. (I)	1.744	54.15	0.371	71.2	0.262	66.6	0.441	58.6
Sch. (II)	2.456	43.9	0.6985	64.4	0.6665	60.0	0.391	31.0
ABSORPTION (PER CENT. OF INTAKE)								
David F.	5.6055	96.0	0.431	84.8	0.6505	93.0	.....	....
Sch. (I)	2.9815	92.5	0.4786	91.7	0.3826	97.6	.....	....
Sch. (II)	5.534	98.6	1.000	92.2	0.9222	82.8	.....	....

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal, or even better than normal, for all the constituents determined. Thus, David F. absorbed 97 per cent. of nitrogen, the normal being 88 to 96 per cent.; retention 50 per cent., the normal being 30 per cent. at this age.

Close scrutiny of the figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism of these constituents. As has been before stated, absorption and retention are unusually good and increased beyond normal, probably indicating a hypernormal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very small amount of actual phosphorus and sulphur in the entire cerebrospinal system, one can understand why, with our present methods, an abnormal elimination of these constituents would fail to be manifested in a study of this disease for short periods. It would be advisable, therefore, to study the disease at intervals during its course, both in its earlier stages in which anabolic changes apparently predominate, and in its later stages in which degenerative and catabolic processes play the important rôle.

PART II.—BY SAMUEL BOOKMAN, PH.D., AND BURRILL B. CROHN, M.D.[8]

This rather rare disease, first identified and studied by Tay and Sachs, has been subjected during the last few years to most searching investigations in regard to its clinical, pathological and histological aspects. The numerous publications throughout the literature are most complete along

these lines; we fail, however, to find any work dealing with the closer examination of the metabolic changes, if any, which accompany the morbid processes which characterize the malady in question. It occurred to us, therefore, to investigate whether the very marked pathological changes which have been repeatedly demonstrated, viz., the universal and generalized degeneration of the neurons, involving all the nerve cells, including the ganglion cells, both central and sympathetic, might not find its concomitant in some abnormal chemical variations.

With this end in view, two cases, D. F. and H. Sch., were subjected to complete metabolism studies. In each instance the patient was put onto a Heubner metabolism bed for four days. The diet was made up into exact duplicates, one of which was fed to the child, the second utilized for analysis. Urine and stool were separated by collecting the stool on a sieve, the urine being allowed to percolate through into another receptacle, and estimated every six hours, being then put on ice to prevent decomposition. The whole stool was collected for each period, sampled and analyzed. The analytical methods employed were as follows:

ANALYTICAL METHODS

Total nitrogen, Kjeldahl method.

Total phosphorus and total sulphur by fusion with sodium hydrate and nitrate.

Chlorin, incineration with sodium, carbonate and nitrate, and titration with silver nitrate. In the urine preformed sulphates in acetic acid solution, and barium chlorid, ethereal sulphate in the filtrate by further boiling with hydrochloric acid.

Total sulphates were determined by direct precipitation in hydrochloric acid solution by barium chlorid.

Neutral sulphur was estimated by difference between total sulphur and total sulphates.

Total phosphates in the urine by titration with uranium acetate (Neubauer's method).

Ammonia by the Folin aeration method.

Total acidity of the urine by titration with N/10 ammonium hydrate, using phenolphthalein as an indicator.

The stool was dried in the water-bath, after addition of alcohol and hydrochloric acid (chlorin in stool not estimated).

CASE 1.—D. F.,[9] male, aged 15 months. One period of four days. Weight at beginning of period 8.12 kg.; weight at end of period, 8.3 kg.; diet, 48 ounces of whole milk per day; calories, 120 per kilogram. Slight but negligible vomiting occurred. (See Table 5.)

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8. From the Laboratory of Physiological Chemistry, Pathological Department, Mt. Sinai Hospital.

The cases on which this study is based, were assigned from the service of Dr. Henry Koplik, attending physician, and Dr. Henry Heiman, associate attending physician to the children's service of Mt. Sinai Hospital. We wish to express our thanks to Drs. Koplik and Heiman for kind cooperation throughout the work in the wards; also to Dr. Theodore Kuttner for valuable assistance in chemical analyses.

9. For the full clinical data of the cases studied, see paper by Heiman, Bookman and Crohn, published in the Transactions of the American Pediatric Society for 1912.

CASE 2.—(Sch.[9]) This patient was subjected to two studies of four days each, with an interval of three weeks between the two periods.

Period I. Age 7½ months; weight at beginning of period, 7.39 kg.; weight at end of period, 7.47 kg.; diet 121 calories per kilogram. (See Table 1.)

Period II. Age 8¼ months; weight at beginning of period, 7.53 kg.; weight at end of period, 7.56 kg. (See Table 6.)

For a more comprehensive comparison of the above tables, we have seen fit to rearrange these in terms of daily average figures (Table 8).

Further, more carefully to analyze the individual factors entering into this metabolism study, we offer the tables and the conclusions derived therefrom (Table 9).

NITROGEN METABOLISM

Case 2 (Sch.) may be compared to the results of Rubner and Heubner[10] in the study of a normal child of the same age. The retention of nitrogen in our case is markedly increased. The absorption is slightly higher in our case than in the one of Rubner and Heubner, although not exceeding normal variations (Table 10).

Case 1 may be compared to Child B of Camerer[11] of approximately the same age and in good health. The retention of nitrogen in our Case 2 on an intake of 5.8 gm. was 47.5 per cent., absorption 96 per cent. In Camerer's case, however, the retention was only 6 per cent. In both of our cases, therefore, absorption and retention are considerably increased. By comparison with Cronheim and Meyer's[12] figures, these deductions are further substantiated (Table 11).

CHLORIN METABOLISM

In the absence of figures for normal children of this age on similar diet, it is impossible to do more than note the high chlorin retention in our cases (Table 12). L. F. Meyer[13] averages several previously published analyses of healthy children on mother's milk and shows but 42 per cent. retained chlorin on an intake of only 20 to 40 per cent. of that of our cases. This emphasizes the fact that the retention in our cases of 31 per cent. to 62 per cent. is remarkably high (Table 13).

PHOSPHORUS METABOLISM

The phosphorus metabolism also is noticeable for its high retention as evidenced by the figures in Table 14. Unfortunately, Keller's[14] figures

10. Rubner and Heubner: Ztschr. f. Biol., 1899, No. 38, p. 315.
11. Camerer: Stoffwechsel des Kindes.
12. Cronheim and Meyer: Biochem. Ztschr., 1908, ix, 80; Ztschr. f. Biol., No. 27, p. 153.
13. L. F. Meyer: Monatschr. f. Kinderh., vii, 104; Ergebn. der inn. Med. u. Kinderh., i, 317.
14. Keller: Ztschr. f. klin. Med., 1898-99, No. 36.

in an article devoted to studies on phosphorus metabolism are not strictly comparable, for the reason that the children he studied were suffering from gastro-intestinal disturbances; neither was the intake noted, nor the excretion of phosphorus in the stool estimated.

A more recent paper by Cronheim and Meyer[12] gives figures for a normal child of about the same age as those investigated by ourselves. The absorption and retention in our cases are even higher than the results obtained by these authors (Table 15).

Keller, as well as Cronheim and Meyer and Rubner and Heubner,[10] have embodied a table of ratios of P_2O_5:N, in their papers. Our figures based on a similar intake of nitrogen show a reduced P_2O_5:N ratio in the urine (Tables 16 and 17).

SULPHUR METABOLISM

The literature contains but little of value on sulphur metabolism in children of this age; proper comparisons of only the output of sulphur can be made by utilizing the figures reported by Freund;[15] these findings, however, were obtained from the study of children suffering from gastro-intestinal disturbances (Table 18).

The absorption and retention of sulphur are both apparently very high, but as no literature exists bearing on this point, we can obviously make no comparisons as regards these results.

In Case D. F., neutral sulphur and ethereal sulphates were lower than the findings in Freund's[15] and Amberg and Morrill's[16] cases of children of about the same ages. We might deduce an increased oxidation of proteid tissue as evidenced by the high preformed sulphate output in its relation to total sulphur and neutral sulphur in the urine (Table 19).

Referring to the work of Schwarz,[17] giving ratios of S: N in the urine, it will be seen from Table 20 that the excretion of S N in our cases is lower than those stated in the findings of this author (for a 5-year-old normal child), the amount of sulphur excreted being reduced in our cases.

GENERAL CONCLUSIONS

Most important in a consideration of the metabolism of amaurotic family idiocy is the stage of the disease and the general condition of nutrition of the patient under investigation. The two children studied by us were both in an early period of this insidious malady; their general

15. Freund: Ztschr. f. Physiol. Chem., No. 29, p. 54.
16. Amberg and Morril: Jahrb. f. Kinderh., No. 69, p. 288.
17. Schwarz: Jahrb. f. Kinderh., 1910, lxxii, part 5, p. 549.

nutrition was good, muscular tissue still very well preserved, and an abundant panniculus adiposus was present. So good was the general health of the children, that during the periods of observation, in both the cases a gain of weight was noted. Thus Sch. gained in the four days of the first investigation 80 gm.; in the second period 30 gm.; Patient D. F. similarly gained 180 gm. In all these instances the nourishment was well taken, the diet consisting of milk diluted in Case 2, and undiluted in Case 1. The caloric intake was in excess of the accepted figures of Heubner (100 calories per kilo per day) to maintain proper nutrition.

From a perusal of the data before us, we are struck by the fact that absorption from the gastro-intestinal tract and retention within the body are normal or even better than normal for all the constituents determined (Table 21).

In view of the fact that this disease is so prominently characterized by a marked and generalized degeneration of nerve cells and nerve tissue, as proven by the very thorough and recent histologic and pathologic studies of Schaffer,[2] Vogt,[3] Brooks,[5] Sachs and Strauss,[6] and others, it would be interesting to discover in the excretions the chemical evidences of the degenerative process which we know is going on. This should be evidenced by some disturbance in the excretion of those elements which are so integral a part of nerve tissue, namely phosphorus and sulphur. In a paper dealing with the chemical analysis of the brain in two cases of amaurotic family idiocy, Mott[7] shows a very distinct change in the relative proportions of simple and neucleoproteins, the latter being diminished, and being replaced by proteins of a simpler composition and with an increased water content. (See Mott's table.)

Close scrutiny of our figures for the intake and output of phosphorus and sulphur does not disclose a marked disturbance in the metabolism of these constituents. As has been stated, absorption and retention are unsually good and increased beyond normal, probably indicating a hypernormal anabolic function occurring at this stage of the disease. However, when one takes into consideration the very slow process of degeneration, extending over a period of months or years, and the very small amount of actual phosphorus and sulphur in the entire cerebrospinal system, one can understand why the daily elimination of these constituents would fail to be manifested in a study of this disease for short periods and with our present methods. It would be advisable, therefore, to study the disease at intervals during its entire course, both in its earlier stages when anabolic changes apparently predominate, and in its later stages when degenerative and catabolic processes play the important rôle.

TABLE 5.—METABOLISM EXPERIMENT IN CASE 1

D. F., period four days; age 15 months; weight 8.125 kg. Nourishment equals 48 ounces of whole milk (raw), equals 975 calories per day or 120 calories per kg. of weight.

INTAKE

Date	N	S	P	Cl
5/3	5.323	0.5447	0.8076	1.4306
5/4	7.302	0.4819	0.7890	1.3470
5/5	4.998	0.4406	0.5024	1.5590
5/6	5.702	0.5676	0.6997	1.7790
Total	23.3250	2.0348	2.7987	6.1156
Daily average	5.831	0.5087	0.6997	1.5290

OUTPUT—URINE

Date	Amount c.c.	Acidity	NH_3	N
5/3	490	123.9	0.1647	2.894
5/4	480	104.8	0.4000	2.432
5/6	480	100.8	0.0618	2.842
5/6	560	alk.	.....	3.167
Total	...	.....	.....	11.335
Daily average	...	.....	.....	2.834

OUTPUT—URINE

Date	Sulphur: Preformed SO_3	Sulphur: Ethereal SO_3	Sulphur: Totals	P_2O_5 as P	Cl
5/3	0.1810	0.00578	0.2295	0.3004	0.653
5/4	0.1664	0.00817	0.1969	0.3379	0.511
5/5	0.2086	0.01262	0.2398	0.3845	0.579
5/6	0.2371	0.00239	0.2632	0.3986	0.581
Total	0.7931	0.05047	0.9294	1.4214	2.324
Daily average	0.1983	0.01262	0.23235	0.35535	0.581

STOOL

	N	S	P
For period	0.902	0.30996	0.1969
Daily average	0.2254	0.07749	0.04922

TABLE 6.—METABOLISM EXPERIMENTS. DAILY SHEET. CASE 2

Sch., aged 7½ months; weight 7.39 kg.; nourishment, per day:

	gm. or c.c.
Whole (raw) milk	960
Water	360
Maltose	45

Caloric value=910 calories or 121 calories per kg. weight.

PERIOD I—INTAKE

Date	N	S	P	Cl
9/19	3.3200	0.3964	0.3933	0.4700
9/20	2.8710	0.4317	0.2758	0.6700
9/31	2.4100	0.4290	0.3124	0.6600
9/22	4.2810	0.8252	0.5918	1.2100
Total	12.8820	2.0823	1.5733	3.0100
Daily average	3.2200	0.5201	0.3930	0.7530

OUTPUT—URINE

Date	Amt. c.c.	Acidity	NH_3	N	S	P_2O_5 as P	Cl
9/19	325	143	0.273	1.2376	0.1104	0.1499	0.4499
9/20	250	102.5	0.292	1.4560	0.1047	0.1357	0.2573
9/21	215	alk.	.....	1.0234	0.1000	0.1017	0.1526
9/22	320	alk.	.....	1.2360	0.11498	0.0966	0.3860
Total	...	.....	.....	4.9530	0.4301	0.4839	1.2458
Daily average	...	.....	.....	1.2382	0.1075	0.1210	0.3115

STOOL

	N	S	P
For period 9/19 to 9/22, 29.5 gm. ..	0.954	0.1697	0.0413
Daily average	0.2385	0.0424	0.0104

TABLE 7.—METABOLISM EXPERIMENT. CASE 2

PERIOD II—INTAKE

Date	N	S	P	Cl
10/13	5.61	0.915	0.936	0.937
10/14	5.34	1.092	0.896	1.312
10/15	5.984	1.191	1.493	1.461
10/16	5.505	1.139	1.144	1.303
Total	22.439	4.337	4.459	5.013
Daily average ..	5.610	1.084	1.115	1.253

OUTPUT—URINE

Date	Amt. c.c.	Acidity	NH_3	N	S	P_2O_5 as P	Cl
10/13	730	73	0.3808	3.026	0.3927	0.1495	0.855
10/14	780	alk.	.....	3.177	0.2986	0.3192	0.886
10/15	750	alk.	.....	3.297	0.2133	0.2445	0.958
10/16	660	alk.	.....	2.810	0.3025	0.3086	0.749
Total	...	...	.....	12.310	1.2071	1.0218	3,448
Daily average	...	...	.....	3.078	0.3020	0.2555	0.862

STOOL

	N	S	P
For period 10/13 to 10/16	0.305	0.336	0.771
Daily average	0.076	0.084	0.1928

TABLE 8.—INTAKE AND OUTPUT—DAILY AVERAGES

INTAKE

	N	S	P	Cl
Sch. I	3.220	0.521	0.393	0.753
Sch. II	5.610	1.084	1.115	1.253
D. F.	5.8310	0.5087	0.6997	1.529

URINE

Sch. I	1.2382	0.1075	0.121	0.2115
Sch. II	3.078	0.302	0.255	0.862
D. F.	2.834	0.23235	0.3553	0.581

STOOL

Sch. I	0.2385	0.0424	0.0104	.....
Sch. II	0.076	0.084	0.1924	.....
D. F.	0.225	0.0775	0.0496	.....

TOTAL OUTPUT

Sch. I	1.4767	0.1499	0.1313	0.3115
Sch. II	3.154	0.388	0.4482	0.862
D. F.	3.059	0.3099	0.4040	0.581

TABLE 9.—NITROGEN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Absorption, Per cent.	Retention	Per cent. of Intake
Sch. I	3.220	1.2382	0.2385	2.9815	92.5	1.744	54.15
Sch. II	5.610	3.078	0.076	5.534	98.6	2.456	43.9
D. F.	5.831	2.834	0.2254	5.6055	96.0	2.772	47.5

TABLE 10.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 2

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Rubner and Heubner,[10] child 7½ months	4.26	3.067	0.281	3.979	93.4	0.912	36.7
Klotz,[18] child 6 months	6.863	4.2625	0.8402	6.0231	87.7	1.76	25.6

TABLE 11.—FIGURES FOR NITROGEN METABOLISM OF NORMAL CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AS CASE 1

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Camerer,[11] child 1 year	5.0	4.0	0.7	4.3	86	0.3	6.0
Cronheim and Meyer,[12] child 6 6 months	4.454	3.182	0.530	3.923	89	0.741	16.7
Cronheim and Meyer, child 6 months	4.454	3.057	0.452	4.001	90	0.945	21.3

TABLE 12.—CHLORIN METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Retention	Per cent.
Sch. I	0.753	0.3115	*	0.441	58.6
Sch. II	1.253	0.862	...	0.391	31
D. F.	1.529	0.581	...	0.948	62

*As HCl was added to stool in the drying process, no Cl estimations were possible.

TABLE 13.—CHLORIN METABOLISM IN HEALTHY CHILDREN (MOTHER'S MILK DIET)

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
L. F. Meyer	0.3217	0.1776	0.0135	0.3162	96	0.1386	42

TABLE 14.—PHOSPHORUS METABOLISM. DAILY AVERAGE

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Sch. I as P	0.3930	0.1210	0.0104	0.3826	97.6	0.262	66.6
as P_2O_5	0.9039	0.2783	0.0239	.....	....	.....	....
Sch. II as P	1.115	0.25545	0.1928	0.9222	82.8	0.66675	60.
as P_2O_5	2.546	0.588	0.4434	.....	....	.....	....
D. F. as P	0.6997	0.35535	0.04922	0.6505	93	0.2951	42.2
as P_2O_5	1.609	0.817	0.1132	.....	....	.....	....

TABLE 15.—PHOSPHORUS METABOLISM IN HEALTHY CHILDREN (SEVERAL AUTHORS) APPROXIMATELY SAME AGES AND WEIGHTS

	Intake	Urine	Stool	Absorption	Per cent.	Retention	Per cent.
Rubner and Heubner,[10] child 7½ mos., as P_2O_5.	2.06	0.589	0.96	1.098	53	0.5079	24
Cronheim and Meyer,[12] child 6 mos.	2.184	0.967	0.733	1.451	66	0.484	22
	1.872	1.069	0.671	1.201	66	0.133	7

18. Klotz: Jahrb. f. Kinderh., 1909, No. 70, p. 1.

TABLE 16.—RATIOS

	RATIOS P_2O_5:N.		
	Intake	Urine	Stool
Sch. I	1: 3.6	1: 4.5	1:10
Sch. II	1: 2.2	1: 5.4	1: 0.17
D. F.	1: 3.65	1: 3.4	1: 2

TABLE 17.—FIGURES FOR RATIO P_2O_5:N FOR HEALTHY CHILDREN (FROM SEVERAL AUTHORS) APPROXIMATELY SAME AGE AND WEIGHT AND DIET

	Intake	Urine	Stool
Rubner and Heubner	1: 2.1	1: 5.2	1: 0.29
Keller		1: 2.1 1: 3.4 1: 3.9	
Cromheim and Meyer	1: 2.1	1: 3.3	1: 0.7
Cronheim and Meyer	1: 2.4	1: 2.8	1: 0.7

TABLE 18.—SULPHUR METABOLISM. DAILY AVERAGE

		Urine						
	Intake	Urine Total S	Preformed SO_3 as S	Ethereal SO_3 as S	Neutral S	Stool	Absorption	Retention
Sch. I	0.521	0.1075				.0424	0.4786	0.3711
							85 %	71.2%
Sch. II	1.084	0.3020				.084	1.000	0.6985
							92.2%	60%
D. F.	0.5087	0.23235	0.1983	0.01262	0.02143	.07749	0.431	0.1989
			85 %	5.43%	9.57%		84.4%	39.1%

TABLE 19.—ANALYSIS OF URINES OF NORMAL CHILDREN FOR SULPHUR CONSTITUENTS. (ALL IN TERMS OF S)

	Total S	Total Sulphates	Per Cent.	Ethereal Sulphates	Per Cent.	Neutral Sulphur	Per Cent.
Amberg and Morril, child 5 mos	0.0747	0.0376	50.3			0.0371	49.7
Freund, child 6½ mos.	0.6717	0.570	86.6	0.0768	9.6	0.100	13.4
Freund, child 4½ mos.	1.032	0.773	75	0.0937	9	0.258	25

TABLE 20.—SHOWING RATIO S:N

	Intake	Urine	Stool
Sch. I	1: 6.2	1:11.6	1: 5.6
Sch. II	1: 5.2	1:10.2	1: 0.9
D. F.	1:11.7	1:12.2	1: 3

TABLE 21.—DAILY AVERAGE (PER CENT OF INTAKE)

	N	N	S	S	P	P	Cl	Cl
		Per Cent.		Per Cent.		Per Cent.		Per Cent.
RETENTION								
Sch. I	1.744	54.15	0.371	71.2	0.262	66.6	0.441	58.6
Sch. II	2.456	43.9	0.6985	64.4	0.6665	60	0.391	31
D. D.	2.772	47.5	0.1989	39.1	0.2951	42.2	0.948	62
ABSORPTION (PER CENT. INTAKE)								
Sch. I	2.9815	92.5	0.4786	91.7	0.3826	97.6		
Sch. II	5.534	98.6	1.000	92.2	0.9222	82.8		
D. F.	5.6055	96	0.431	84.8	0.6535	93		

PROGRESS IN PEDIATRICS

A SUMMARY OF THE RECENT LITERATURE ON ORTHOSTATIC ALBUMINURIA

MURRAY H. BASS, M.D.
NEW YORK

In May, 1910, D. R. Hooker[1] published a critical summary of the literature on the subject of orthostatic albuminuria. In this excellent paper in which he gives a concise, comprehensive and systematic review of the various theories which have been advanced to explain this type of albuminuria, he divides the subject-matter into three periods. The first period deals with the work of Leube, Senator, Posner, Ultzman, Gull, Moxon and others, who first laid emphasis on the presence of albumin in the urine of healthy individuals; it includes Pavy, who, in 1885, was the first to show the influence of the upright posture, and ends with the paper of Dubreuilh, in 1887. The second period extends from 1887 to the appearance of Edel's researches in 1904. In this period falls some of Teissier's work in which the name "orthostatic" is first applied. "This period is characterized by the development of scientific interest and a strong effort to define the etiology of albuminuria by means other than simple clinical observation." The third period includes the work of Teissier, who first emphasized the occurrence of true orthostatic albuminuria where no etiologic factor can be found, and the cause of which he believes to lie in the semipermeability of the glomeruli, due to faulty development. In this period also appear the researches of Erlanger and Hooker, who showed the relationship between the vasomotor system, especially the pulse-pressure and albuminuria; and also the work of Langstein, who first studied the metabolism of orthostatic albuminurics and who published the first autopsy on an undoubted case.

LORDOSIS AS A CAUSE OF ALBUMINURIA

Since the publication of Hooker's review, however, the subject of orthostatic albuminuria has received added interest and much new work has appeared as the result of the publishing of Ludwig Jehle's monograph on Lordotic Albuminuria.[2] Jehle believes the appearance of albumin in the urine while the individual is in the upright position and its disappearance on lying down is due to a venous hyperemia of the

1. Hooker, D. R.: Arch. Int. Med., 1910, v, 491.
2. Jehle, L.: Die Lordotische Albuminurie. Leipzig and Wien, 1909.

kidney brought about by a faulty position of the lumbar spine. He observed that orthostatic albuminurics showed a lordosis in the region of the first and second lumbar vertebræ. He bases his views on the examination of a large number (300) of children and attempts to show that the lordosis is practically the only factor of importance. By causing an artificial lordotic position of the spine he can produce albuminuria with the child on its back, while on the other hand, by the application of a plaster jacket so as to correct the lordosis, he is able to make the urine albumin-free even when the child is up and about. By the use of a specially constructed apparatus he can reproduce on paper the exact contour of the spinal column and can show that those children that had previously been diagnosed as orthostatic albuminurics all present the typical lordosis. Conversely children whose vertebral columns are straight fail to show albumin in their urine.

Jehle's contention that the lordotic lumbar spine is the chief cause of the albuminuria has been corroborated by some investigators and denied by a few. Fischl[3] agrees with Jehle in considering the lordosis of great importance, but he believes that there is still another factor to be dealt with in the shape of a peculiar weakness of the kidney which permits the lordotic posture to produce albuminuria. This is especially emphasized in the difficulty with which albuminuria is obtained in normal children by placing them in artificial lordosis. He is not inclined to attribute too much importance to the vasomotor theory, since the results of blood-pressure readings, sphygmograms and *x*-ray examinations have varied greatly with different authors. He concludes "that under the influence of a lordosis, limited to the upper lumbar column and appearing with the body in certain positions, a congestion of the kidneys is brought about which, in the presence of an existing disposition of these organs to mechanical influences, leads to an excretion of albumin and formed elements, the intensity of this excretion depending directly on the grade and duration of the procedure." He therefore would name the condition "*Lordotische dispositionsalbuminurie.*"

M. Englander,[4] in reporting a case in an adult, takes this same standpoint, that there must be a second etiologic factor besides the lordosis. Hamburger[5] in the same way, while conceding the importance of the purely mechanical factor, points out that vasomotor instability must play a part, and that it is chiefly in vasoneurotics that lordosis produces albuminuria. He emphasizes the fact that the same individual reacts to lordosis at one time with an albuminuria, at another time without it.

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3. Fischl, R.: Arch. f. Kinderh., 1909, lii, 261.
4. Englander, M.: "Ein Fall von orthotischer Albuminurie." Mitt. der Gesellsch., f. inn. Med. u. Kinderh. in Wien, 1911, p. 166.

Fischl[6] has, moreover, confirmed the importance of lordosis by animal experiments. Rabbits, when kept in exaggerated lordosis, showed albumin, casts and red blood-cells. Food given seemed to influence the results. Repeated experimental lordosis may lead to nephritis and death. The kidneys of such cases pathologically examined resemble the kidneys of pædonephritis. In dogs, also, albumin appeared after lordosis. The lordosis seems to act mechanically and not reflexly, since it also provokes albuminuria when the whole experiment is carried on in narcosis. The general blood-pressure does not seem to have much influence on the excretion of the albumin, but the oncometer shows an increase in the volume of the kidney, and as increase in the arterial flow can be excluded, this probably means a slowing of the blood-current in the kidney.

Together with Wohrizek,[7] Fischl has used a corset, which cures not only the albuminuria, but also the attending symptoms.

Bruck[8] also emphasizes the importance of lordosis as a causative factor, finding it in almost every case of orthostatic albuminuria. He was, however, in contradistinction to Jehle, unable to obtain albuminuria in the prone position no matter how great an artificial lordosis he produced. He took normal non-lordotic children and put them in lordotic position by letting them kneel. Of the forty-four children thus examined, 18 per cent. showed albumin. Some of these positive cases were absolutely normal children, some had organic disease, some were markedly neuropathic. In general, he concludes that "albuminuria provocativa orthostatica" (i. e., albuminuria which does not appear until it is provoked by placing the child in an upright lordotic position), though an interesting condition, cannot in any manner be used to differentiate various types of children nor to distinguish various degrees of renal sufficiency.

B. Vas[9] reports observations on 150 girls ranging in age from 9 to 14 years. Of these, sixty-two had albuminuria, and twenty-six of these showed the orthostatic variety. Examining these twenty-six he found albumin together with lordosis in fifteen cases; albumin without lordosis in eleven cases. He also found nine cases with lordosis, but without albuminuria. He concludes that at puberty orthostatic albuminuria occurs about as often with lordosis as without it. Lordosis without albuminuria also occurs. It cannot be regarded as the sole cause of orthostatic albuminuria.

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5. Hamburger, F.: Wien. klin. Wchnschr., Feb. 15, 1912, No. 7.

6. Fischl, R.: Ueber mechanische Hervorrufung von Albuminurie u. Erzeugung von Nephritis bei Kaninchen, Monatschr. f. Kinderh., 1909, viii, 388, and 1910, p. 641.

7. Wohrizek: Med. Klin., May 1, 1910.

8. Bruck, A. W.: Ueber Albuminuria Provocativa Orthostatica, München. med. Wchnschr., 1908, No. 44, p. 2271.

9. Vas, B.: Zur Frage der lordotischen Albuminurie, Deutsch. med. Wchnschr., 1909, No. 34.

There seems to be a great difference of opinion as to whether the assumption of the lordotic position while lying down gives rise to albuminuria or not. Bury and Ward[10] report a case of chorea and postural albuminuria, in which they could get only inconstant traces of albumin when lordosis was assumed with the child in bed. Hutinel[11] reports contradictory results. Turrettini,[12] on the other hand, finds that exaggeration of the lumbar lordosis causes the appearance of albumin in all cases of orthostatic albuminuria regardless of the position — whether horizontal or standing. He finds that even while standing the assumption of a position with the trunk bent slightly forward is sufficient to remove the albumin again. F. Parkes Weber,[13] and also Nobécourt,[14] reporting cases, also concede that lordosis has a marked effect, but that nevertheless there are still other causative factors at work.

Ebstein[15] calls attention to an article written by Bartels in 1875, in which he reports a case of pseudohypertrophic muscular dystrophy with marked lordosis and an albuminuria of the typical orthostatic variety. Goldreich[16] reports a similar case in a child, aged 9 years, in whom the same muscular disease was present, accompanied by lordosis and orthostatic albuminuria. Schreiber,[17] on the other hand, describes thirty cases of coxalgia with lordosis, none of which showed albuminuria; while Pechowitsch[18] found that in a class of thirty lordotic children who were being treated by Klapp's creeping exercises, five showed albuminuria. All of these five showed less albumin immediately after treatment by exercises which diminished their lordosis.

A very good exposition of the relationship of lordosis to albuminuria is presented by Pincherle,[19] and is worth reporting in more detail. He examined over 100 children and comes to the following conclusions: Undoubtedly a lordosis not too extreme in character and involving the

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10. Bury and Ward: A Case of Postural Albuminuria in a Boy the Subject of Chorea, Lancet, London, Jan. 1, 1910.

11. Hutinel: Albuminurie orthostatique, Rev. gén. de clin. et de therap., 1910, p. 372.

12. Turrettini, G.: Etude clinique de l'albuminurie dite orthostatique, Rev. méd. de la Suisse romande, 1910, No. 30, p. 767.

13. Weber, F. P.: Remarks on Orthostatic albuminuria, Brit. Jour. of Child. Dis., September, 1911.

14. Nobécourt: Albuminurie orthostatique Fonctionelle, Gaz. d. hôp., 1910, p. 313.

15. Ebstein, E.: Juvenile Dystrophie und lordotische Albuminurie im Kindesalter, Ztschr. f. Kinderh., 1911, No. 3.

16. Goldreich, A.: Dystrophia musculorum progressiva mit lordotischer Albuminurie, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. in Wien, 1911, No. 7, p. 135.

17. Schreiber, M. G.: Critique de la Theorie Lordotique de l'Albuminurie Orthostatique, Presse méd., Oct. 20, 1909.

18. Pechowitsch, G.: Einfluss der Kriegsübungen auf die lordotische Albuminurie, Deutsch. med. Wchnschr., Oct. 27, 1910.

19. Pincherle: Riv. di clin. pediat., 1911. Reviewed in the Monatschr. f. Kinderh., 1912, No. 11, p. 508.

upper segment of the lumbar column, is a marked factor in causing albuminuria. There is no direct relationship between the grade of the lordosis and the albuminuria. In some individuals with a marked lordosis it was impossible even with artificial exaggeration of the deformity to cause albumin to appear. Artificial lordosis of moderate grade, however, in most cases results in albuminuria, whether in the vertical or the horizontal position. This reaction to posture differs; in normal individuals the albumin excreted is minimal in amount; in those predisposed (nephritics, tuberculous individuals) it is much greater in amount. The reaction to lordosis is characterized by albuminuria, oliguria and the appearance of formed elements in the urine; it varies with the mechanical factor, the general condition of the subject and with the local condition in the kidney. The traumatic influence of the lordosis may show the weakness left by previous disease, and the reaction to posture may therefore, as pointed out by Nothman and Devoto, be useful as a functional renal test. Attention to an existing lordosis is often an important factor in curing an albuminuria. The damaging influence of lordosis on the kidney is shown by animal experiments in which staphylococci were injected in control and into lordotic rabbits, with the result that the latter got very much more severe renal lesions.

Goetzky,[20] after careful examination of a number of children over a considerable period of time, is inclined to deny the significance of lordosis as the etiologic factor in true orthostatic albuminuria. He admits that by artificial lordosis one is able to produce an albuminuria in almost every child, whether healthy or ill, but he cites orthostatic cases who show no trace of lordosis and also points to the fact that the degree of lordosis and the amount of albumin are not at all proportional. The albumin in cases of orthostatic albuminuria disappears almost immediately when the patient assumes the horizontal position, whereas after artificial lordosis albuminuria may persist for five or six hours.

OTHER MECHANICAL FACTORS

Other mechanical factors besides the lordosis have been pointed out as causes of the albuminuria. Eppinger,[21] in reporting the case of an adult suffering from orthostatic albuminuria, shows that the distance between the upper border of the heart and the diaphragm, as revealed by the *x*-rays, is increased; that is to say, the position of the diaphragm is very low. As a result of this, when the patient is in the upright position, there is tension on the inferior vena cava and consequent stasis in the renal

20. Goetzky, F.: Zur Kenntnis der orthotischen Albuminurie, Inaugural dissertation, Berlin, 1910.

21. Eppinger: Die Function des Zwerchfells beim Zustandekommen der orthostatischen Albuminurie, Mitt. d. Gesellsch. f. inn. Med. u. Kinderh. in Wien, 1912, No. 6.

veins. Eppinger believes that the disappearance of the albumin after the application of an abdominal binder is due to the resulting elevation of the diaphragm.

Vorpahl[22] describes a 12-year old girl with orthostatic albuminuria who presented slight lordosis, but marked left lumbar scoliosis. In the sitting posture, which overcame the lordosis, albumin persisted. Ureteral catheterization showed that the albumin came from only the right kidney, evidently as a result of the scoliosis.

Mayer[23] reports an orthostatic case in an adult in whom ureteral catheterization also showed unilateral albuminuria.

Piesen[24] comments on the frequency of orthostatic albuminuria in school children who are forced to sit with their arms folded behind their backs.

A number of cases have been reported (Niviere,[25] Mosny,[26] Lury[27]), in which orthostatic albuminuria seemed to be dependent on movable kidney, as was long ago pointed out by Sutherland.

RELATIONSHIP OF ORTHOSTATIC ALBUMINURIA TO ACUTE DISEASES, ESPECIALLY TO SCARLET FEVER

Stephanie Weiss-Eder[28] let children suffering from scarlet fever kneel so as to produce lordosis for ten to twenty-five minutes. She repeated this procedure every two to seven days, using only children who, in the non-lordotic position, showed no albumin. Of forty children thus examined, twenty-three showed albumin and seventeen showed none. In none of the twenty-three positive cases did a nephritis follow. One child, which in lordosis was continuously negative, developed a nephritis on the twenty-third day. The author concludes that (1) children, who in convalescence from scarlet fever have orthostatic albuminuria, are not more disposed to nephritis than other children; (2) children convalescent from scarlet fever having nephritis often show orthostatic albuminuria which may be due to weak muscles; (3) 57.5 per cent. of the children convalescent from scarlet fever show orthostatic albuminuria.

These results (and also those of a number of other authors) are not in accord with the findings of Nothman,[29] who believes that the artificial lordotic position may be used to give information concerning the func-

22. Vorpahl, K.: Ueber einseitige orthostatische Albuminurie, Berl. klin. Wchnschr., May 2, 1910, p. 827.

23. Mayer, K.: Einseitige Zyklische-orthotische Albuminurie, Ztschr. f. gynäkolog. Uro., 1909, i, 229.

24. Piesen: Wien. klin. Wchnschr., Jan. 5, 1911.

25. Niviere: Soc. méd. d. hôp. de Paris, 1904.

26. Mosny: Soc. méd. d. hôp. de Paris, 1904.

27. Lury: Jahrb. f. Kinderh., December, 1910.

28. Weiss-Eder, S.: Orthotische Albuminurie und Scharlachnephritis, Wien. med. Wchnschr., 1909, No. 18, p. 977.

tional efficiency of the kidney. He found that in twelve out of thirteen cases of scarlet fever in which at an earlier date the lordotic experiment was positive, albumin later on appeared in the urine; but in those in whom lordosis did not cause albuminuria, albumin never appeared spontaneously later on. He thinks that just as nephritis may terminate in orthostatic albuminuria, so conversely an orthostatic albuminuria may be the first sign of a nephritis, and that on this account convalescents from scarlet fever showing albumin after kneeling need particular watching in respect to developing nephritis.

Schick[30] comments on the good prognosis of orthostatic albuminuria following scarlet fever. He refers to Jehle, who examined seventeen children in various stages of scarlet fever. In twelve of these there was marked albuminuria during lordotic positions whether upright or prone, but in none of them did a nephritis supervene.

Le Noir[31] had a patient with orthostatic albuminuria who passed through an attack of typhoid and then one of scarlet fever without developing symptoms of renal involvement. Dufour[32] reports a similar case in which previous orthostatic albuminuria followed by scarlet fever showed no sign of nephritis. Turrettini[33] describes similar cases. In a series of fifty scarlet fever cases reported by him, four had signs of nephritis. In these four children, the creation of an artificial lordosis by placing a pillow beneath the lumbar spine, caused a recrudescence of the nephritis lasting several days.

RELATION TO TUBERCULOSIS

The relationship between tuberculosis and albuminuria has long been pointed out especially by the French, who speak of a pretuberculous albuminuria. Lately various French observers have emphasized that orthostatic albuminuria occurs more often in children with a tuberculous family history. F. Parkes Weber,[13] on the other hand, believes that it is merely the similarity in the clinical pictures presented by orthostatic albuminurics and tuberculous individuals (tall, thin, flat-chested individuals; winged scapulæ, etc.), which has given rise to the opinion that the albuminuria may be the result of the infection. Goetzky[20] in a large number of cases was also unable to find a greater number of positive Pirquet reactions in children suffering from orthostatic albuminuria than in control children.

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29. Nothman, H.: Ueber lordotische Albuminurie, Arch. f. Kinderh., 1909, No. 49, p. 216.

30. Escherich and Schick: Sharlach, 1912, Nothnagel's System, p. 141.

31. Le Noir: Quoted by Courcoux, Paris méd., 1910-11, p. 363.

32. Dufour, H.: Soc. méd. d. hôp., Feb. 2, 1906.

33. Turrettini, G.: De la Pathogenie de l'Albuminurie dite Orthostatique, Rev. de Méd., September, 1909, p. 694.

Ludke and Sturm,[34] however, conclude from a study of 140 cases that a large percentage of individuals with pulmonary tuberculosis show albumin in their urine after being on their feet for one hour. In those cases in which no albumin appeared, a very small injection of tuberculin resulted in an albuminuria in more than half of the cases. The authors believe that orthostatic albuminuria can be used as a diagnostic aid in early tuberculosis.

ORTHOSTATIC ALBUMINURIA AND RENAL SUFFICIENCY

Considerable confusion exists as to the relationship between orthostatic albuminuria and nephritis. Heubner and his school believe that a case may be classed as orthostatic albuminuria only if the presence of albumin conforms strictly to the posture of the child and if formed elements are continuously absent. Goetzky, in his monograph before referred to, published from Heubner's clinic, divides his cases into: 1. Orthostatic albuminurics, in whom there are never any casts and in whom the presence of albumin is always dependent on posture. 2. Orthostatic nephritics, in whom casts may appear, but who seem much influenced by posture. 3. Cases in which the albuminuria is not strictly dependent on posture and which may show casts. (These last are cases of chronic pædonephritis.) He still adheres to the belief that the appearance of casts and red blood cells signifies the existence of a nephritis, and that therefore Jehle's contention that formed elements appear after artificial lordosis is true only because Jehle was dealing with kidneys the seat of previous inflammation. In other words, many of Jehle's experiments were performed not on normal children, but on chronic nephritics of the type pointed out by Heubner as characterized by no subjective or objective symptoms excepting the excretion of urine containing albumin and occasional casts.

The French school, following the lead of Teissier, also insist on a rigid classification separating the true orthostatic albuminuria from the other forms. Nobécourt[14] reports cases in which tests for functional efficiency of the kidney (methylene-blue and NaCl excretion) were normal. He believes that orthostatic albuminuria is due to changes in the blood-supply of the kidneys. According to Springer,[35] the condition is due probably to a relative insufficiency of the kidney caused by rapid growth of the rest of the body, with which the growth of the kidney is unable to keep pace. In favor of this view are the following facts: The disease appears as a rule at or near puberty. It is frequently accompanied by

34. Ludke, H., and Sturm, J.: Die orthotische Albuminurie bei Tuberculose, München. med. Wchnschr., May 9, 1911.

35. Springer, M.: Albuminurie Physiologique et Orthostatique, Presse méd., July 29, 1911.

symptoms of vasomotor insufficiency. It tends to heal spontaneously when the time of rapid growth is past. Similar views are put forth by Turrettini,[33] who believes that true orthostatic albuminuria is due to lordosis acting on a kidney insufficient because of rapid growth.

Courcoux[36] gives a very clear classification of the cases, dividing them as follows: 1. True, so-called functional, albuminurias, usually in tall, thin children, 10 to 15 years of age; lordotic or scoliotic; emotional, easily tired, complaining of headaches, and showing a neuropathic heredity. Their complaints point to vasomotor instability as shown by cold, clammy extremities, lability of the pulse, palpitation, etc. Casts are never found in their urine. Albuminuria is most marked toward the end of the morning. Functional renal tests are normal. Outcome of the disease is good and the kidneys are not more susceptible to damage even by scarlet fever. 2. Orthostatic nephritic albuminuria. This is the commonest type. It also usually occurs in children (a) as the result of an infection, (b) as the preliminary symptoms of a chronic nephritis. These cases may resemble the first variety, but functional renal tests show insufficiency. As a result of errors in diet or fatigue, continuous albuminuria may occur. The urine shows diminution in the excretion of nitrogen, chlorids and phosphates, and reveals an oliguria in the upright position. When frequently examined casts are found. 3. So-called associated orthostatic albuminuria—these are cases associated with gastro-intestinal disturbances. Courcoux believes that in any of these three classes albumin appears in the upright posture owing to diminished blood-supply to the kidney, and that this diminution occurs especially commonly in persons showing vasomotor instability.

In a series of articles Linossier and Lemoine[37] lay great stress on the oliguria which occurs in cases of orthostatic albuminuria. By a number of careful researches they come to the conclusion that the functional efficiency of the kidneys of such patients can best be appreciated by the measurement of this oliguria. They find that in a kidney the seat of very slight disease, the upright posture causes an oliguria accompanied by a diminution in the excretion of chlorids, urea and phosphates. This orthostatic oliguria in its more advanced stage may become an albuminuria. Normal persons show no orthostatic oliguria. The authors conclude that the oliguria and the consequent albuminuria are caused by a slowing of the renal circulation brought about by the upright posture; and that

36. Courcoux: Die Orthostatischen Albuminurien. Translated from Paris méd. by G. Steinitz in Allg. Wien. med. Ztg., 1911, p. 324.

37. Linossier, G., and Lemoine, G. H.: Le mecanisme de l'albuminurie et de l'oligurie orthostatique, Presse méd. Mar. 24, 1909; also Soc. méd. d. hôp., Mar. 19, 1909, p. 565.

they are due to some alteration in the kidney, probably more of a functional than an organic nature.

NATURE OF THE ALBUMINOUS PRECIPITATE

For a number of years the fact has been known that in the urine of orthostatic albuminuria cases an abundant precipitate is thrown down on the addition of acetic acid in the cold. The nature of this precipitate has been disputed. Langstein[38] believed it was probably of the nature of euglobulin, and that on account of the very small amounts of phosphorus it contained, it was not a nucleoproteid as had been supposed. Lately Pollitzer[39] has published work which corroborates the theory of Moerner that the precipitate is caused by a combination of serum-albumin and chondroitin-sulfuric acid. Pollitzer used serum-albumin as a titration fluid and showed that when this was added to normal or to nephritic urine, only a very faint opalescence appeared. When, however, it was added to the evening urines of orthostatic albuminuria cases a heavy precipitate resulted. This evidently means that there is present in such urine a body, possibly chondroitin-sulfuric acid, which in the presence of acetic acid in the cold, unites with serum-albumin to form an insoluble compound.

Giffhorn[40] found that in the urines of infants suffering from malnutrition or dyspeptic disturbances a precipitate often appeared on adding acetic acid in the cold. However, he does not believe that its presence is of much significance.

PROGNOSIS

In general, recent literature lays stress on the good prognosis of true orthostatic albuminuria. In a discussion of the after-history of orthostatic cases at the Royal Society[41] in London, numerous examples of the condition were cited to show that its prognosis was excellent. Hutinel[11] and F. P. Weber[13] lay particular stress on the good outcome of the disease, the latter believing that even the presence of an occasional hyaline cast is of no significance. This is contrary to the views expressed by Heubner and his adherents, who, as has been mentioned above, believe that the presence of casts speaks for a nephritis and therefore for a more

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38. Langstein, L.: Die Albuminurien älterer Kinder, Monograph, Leipzig, 1907.

39. Pollitzer, H.: Ueber die Natur u. die Rolle des durch Essigsäure fällbaren Eiweisskörpers bei orthotischen Albuminurien, Deutsch. med. Wchnschr., March 14, 1912.

40. Giffhorn: Beitrag zur Klinischen Bedeutung des durch Essigsäure fällbaren Eiweisskörpers im Urin der Säuglinge. Monatschr. f. Kinderh., 1911, p. 648.

41. The After-History of the Albuminuria of Adolescence. Brit. Med. Jour., May 6 and 13, 1911.

serious prognosis. In this connection it is of interest that recently C. Posner[42] has expressed his view that occasional hyaline casts may be present without a real inflammation of the kidney.

TREATMENT

In all the recent writings nothing has been added to the therapeutics of orthostatic albuminuria with the exception of mechanical and gymnastic measures used to overcome any existing lordosis, as referred to above.

54 West Ninety-First Street.

METABOLISM AND NUTRITION

Medical Certification of Milk; Its Advantages in Infant Feeding

(G. C. Mosher: Dietetic and Hygienic Gazette, March, 1912)

The most essential feature of the infant feeding reform, in the opinion of Mosher, is education; education of the profession and through it of the nurses and mothers. When it is stated in a newspaper article that a certain specimen of milk contains 5,000,000 bacteria to the cubic centimeter, few people stop to consider what it signifies, he says; but where we translate the language to the vernacular, and say that the specks in the bottom of the milk bottle are cow manure and dead epidermis from the cow's body, falling into the milk-pail during the faulty process of milking, it becomes more tangible and the enormity of the offense appeals to any layman. In every community there has often been sold milk at a high price under the name of "baby milk," or some such title as would indicate the milk to have some special qualification. As a matter of fact, these claims are frequently not based on any more ground than that the mothers of children fed on this milk have confidence in the dairyman, and pay him the excess price because of this confidence, the milk usually having been taken from the same can as that called commercial or table milk. In other words, the child fed on this milk was usually running the same risks as every other baby fed on herd milk, and the basis of security which the mother imagined was a real protection because she paid for the "baby milk" a price which often she could not afford, caused her to become the victim of misplaced confidence.

Some of the points of the series of minimum requirements adopted by the Kansas City Pure Milk Commission are that the barns shall be of sanitary construction, with a proper area of cubic feet for each animal; a system of ventilation to insure pure air in the stable; pure water-supply; cement floors and trenches, to be flushed daily with running water. The building must be ceiled to prevent accumulation of dust over the cows. The cows are quarantined until passed on by the commission veterinarian before being added to the herd. The fresh cow is not to be milked for use in the milk-supply until about the fifth day after her delivery. The milk is discarded six weeks before her next calving; cows are fed after milking, so as to avoid dust during milking. The cows are all washed over the udder and flank rubbed dry; then a chain passed

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42. Posner, C.: Die diagnostische u. prognostische Bedeutung der Harnsedimente. Samml. Zwangloser Abhand. a. d. Grenzgeb. d. Verdauungskr. u. Stoffwechsel, 1912, iii, No. 7.

under their necks to prevent their lying down until after milking is finished, to avoid soiling the udder. Sanitary suits are worn by the milkers, and the hands must be washed and wiped dry before each milking. The pails used have small openings in the top to prevent the entrance of any foreign material. The first few spurts are always discarded, which insures a diminution of bacterial contamination. The milk of each cow is at once carried to the dairy house, and not allowed to remain in the warm stable after being drawn. The milk is to be bottled under most careful auspices and sealed by the official seal of the commission, which guarantees it to the consumer. The commission has adopted as a maximum bacterial count 30,000 to the cubic centimeter for all bacteria. Certified milk is not treated in any way to preserve it. Nothing is added to it or taken from it. It is simply pure milk, kept from its origin until the delivery to the customer.

F. C. ZAPFFE.

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